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Surgical mesh for inguinal hernia repair

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Abbreviations

AAS	Activities Assessment Scale
BHS	British Hernia Society
BPI	Brief Pain Inventory
CADTH	Canadian Agency for Drugs and Technologies in Health
CI	Confidence interval
EHS	European Hernia Society
HTA	Health technology assessment
IEHS	International Endohernia Society
MAS	Medical Advisory Secretariat
MRI	Magnetic resonance imaging
NIHR	National Institute for health Research
POP	Pelvic organ prolapse
QALY	Quality-adjusted life year
QoL	Quality of life
RCT	Randomized controlled trial
R&D	Research and development
RR	Risk ratio
SF-36	Short-form 36
SUI	Stress urinary incontinence
TAPP	Transabdominal preperitoneal
TEP	Totally extraperitoneal
TIPP	Transinguinal preperitoneal

Executive Summary

Purpose

This report summarizes the findings of reviews of efficacy and safety of polypropylene surgical mesh for the treatment of inguinal hernia.

Background

“Surgical mesh” refers to a flexible material implant used to support and repair soft tissues in the body. Meshes may be made of biological material such as porcine dermis, autologous tissue from the patient’s body, absorbable synthetic material, or non-absorbable synthetic material like polypropylene. Mesh is a common and long-standing method of hernia repair.

Methods

The following methodological approaches were used to gather and synthesize the available evidence:

I. Environmental scan of licensure of surgical mesh for inguinal hernia across Canada and internationally
II. Review of health technology assessments of surgical mesh for inguinal hernia
III. Review of guidelines and best practice recommendations for surgical mesh
IV. Systematic review of safety and clinical effectiveness of surgical mesh for inguinal hernia

Key Findings

Environmental Scan of Licensure of Surgical Mesh for Inguinal Hernia across Canada and Internationally

Many inguinal hernia meshes are available for implantation in Canada and the United States. No broad actions against the use of mesh for inguinal hernia repair have been taken by the countries included in this analysis; however, certain products have been banned in Canada and the United States. Surgical meshes for urogynaecological indications have been subject to scrutiny due to high complication rates; while hernia meshes are similar in construction, there is considerably less concern over the use of meshes for hernia repair. The new Action Plan on medical devices

published by Health Canada in 2018 will intensify the pre-market approval process, increase post-market surveillance, and enhance the transparency of approval and surveillance of medical devices, including surgical synthetic mesh for inguinal hernia repair.

Review of Guidelines and Best Practice Recommendations for Surgical Mesh

For repair of inguinal hernia, the HerniaSurge Group and BHS both recommend the use of surgical mesh, particularly using a laparoscopic/laparo-endoscopic technique. TAPP and TEP are generally regarded as having comparable patient outcomes and the choice of technique should be based on the surgeon's expertise. Recommendations from the HerniaSurge Group regarding mesh material use include not selecting mesh solely based on terms "lightweight" or "heavyweight."

Review of Health Technology Assessments of Surgical Mesh for Inguinal Hernia

Two inguinal hernia HTAs were identified; one HTA found that open preperitoneal mesh repair was more clinically effective than Lichtenstein mesh repair; the other HTA found that laparoscopic repair was more clinically effective than open mesh repair. Specific recommendations regarding the use of surgical mesh for inguinal hernia were not provided; additional research was deemed to be warranted.

Systematic Review of Clinical Effectiveness of Surgical Mesh for Inguinal Hernia

Twenty unique RCTs and three follow-up studies were identified that evaluated the effectiveness of synthetic surgical mesh for inguinal hernia against comparators of interest. Nineteen studies compared synthetic mesh to suture repair and four compared synthetic mesh to porcine mesh. Studies ranged from 1 to 87.6 months of maximum follow-up time, and 12 months was the most common follow-up time-point. Results suggest that the risk of recurrence at 6-12 months is 6% smaller with synthetic mesh than with porcine mesh (effect is not significant); and that the risk of recurrence at <1 year is 1% greater with synthetic mesh than with suture repair but is 2% smaller at 1-2 years, 3-5 years, and ≥5 years (effects are not significant and the latter three are associated with moderate-to-substantial heterogeneity and should be interpreted with caution). Meta-analyses of complications suggest that synthetic mesh is not significantly different from suture repair with respect to the risk of infection, pain, hematoma, seroma, testicular atrophy, urinary retention, and neurological complications (0-3% risk differences with no statistical significance),

and not significantly different from porcine mesh with respect to risk of infection, pain, hematoma, and seroma (0-8% risk differences with no statistical significance). Overall, synthetic surgical mesh appears to have a similar efficacy and safety profile to suture repair and porcine mesh.

Conclusions

Surgical mesh, particularly using a laparoscopic/laparo-endoscopic technique, was recommended for inguinal hernia repair by the two guidelines identified by this review. The environmental scan has not identified any broad actions against surgical mesh for inguinal hernia in Canada or internationally, although some hernia meshes have been banned since 2006 for safety reasons. A system for monitoring long-term complications associated with medical devices, including surgical mesh repair for inguinal hernia, remains necessary and is in the process of being established by Health Canada.

With respect to recurrence rates, a review of the published scientific literature on synthetic surgical mesh and its comparators for inguinal hernia found similar efficacy of synthetic mesh to porcine mesh and suture repair (although this effect needs to be interpreted with caution due to heterogeneity in the meta-analysis). Risk profile of complications for synthetic surgical mesh was similar to suture repair and porcine mesh. Analyses of the literature were limited by inconsistency in follow-up times and sample sizes across RCTs, which likely contributed to the heterogeneity in the recurrence analysis. Furthermore, validated QoL data were scarce.

1 Purpose of this Health Technology Assessment

The purpose of this health technology assessment (HTA) is to synthesize current evidence on the use of synthetic surgical mesh for treatment of inguinal hernia. This report summarizes the evidence in the literature on the clinical effectiveness and safety of mesh products for this condition, and the current context in Canada and globally. The evidence is synthesized to emphasize the safety profile of mesh products.

2 Research Question and Research Objectives

The primary research questions are:

1. Is the use of polypropylene surgical mesh as clinically effective as alternative products in the treatment of inguinal hernia? In particular:
    a. What is the safety profile and complication rate of polypropylene surgical mesh?
    b. What are the time horizons for the included studies and is there sufficient evidence to support the same conclusions over the long-term?

3 Overview of Approach

A variety of methodological approaches were used to gather and synthesize the available evidence in order to address the primary research questions. The following methodologies were used:

I. Environmental scan of licensure of surgical mesh for inguinal hernia across Canada and internationally
II. Review of health technology assessments of surgical mesh for inguinal hernia
III. Review of guidelines and best practice recommendations for surgical mesh
IV. Systematic review of safety and clinical effectiveness of surgical mesh for inguinal hernia

4 Background

4.1 Surgical Mesh

4.1.1 Description of Mesh

"Surgical mesh" refers to a flexible material implant used to support and repair soft tissues in the body. Polypropylene meshes were initially used over fifty years ago to repair abdominal hernias by reinforcing the body wall to prevent recurrence. Recently, mesh has also been used to support pelvic organs to treat pelvic organ prolapse (POP) and stress urinary incontinence (SUI).[1]

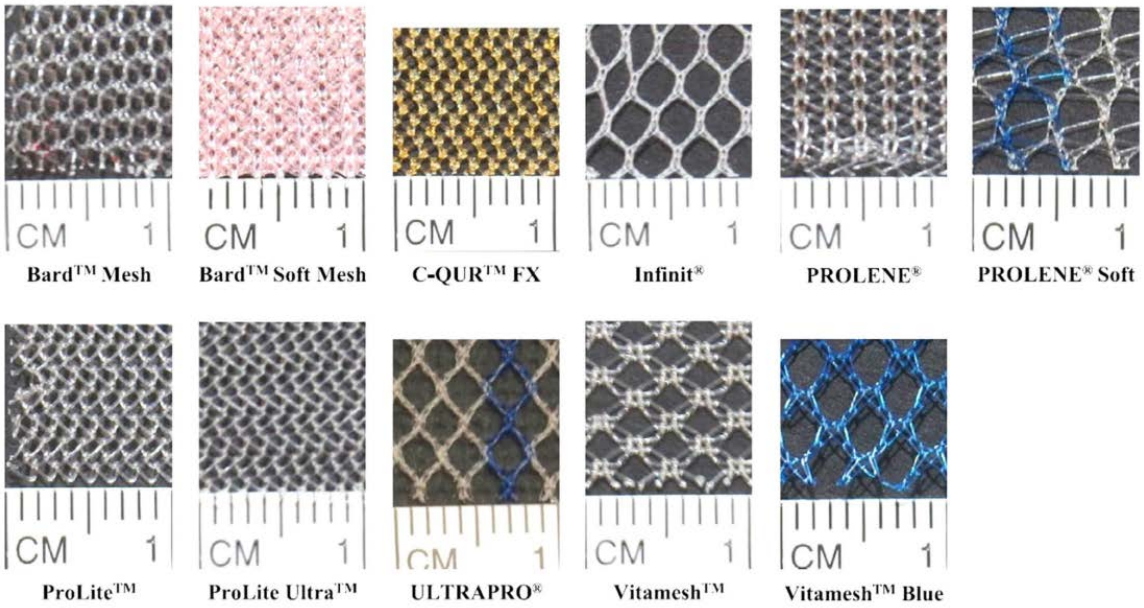
Meshes may be made of biological materials such porcine dermis, cadaveric fascia, or autologous fascial tissue harvested from the patient themselves. Absorbable synthetic meshes are also available, although they are not as effective at preventing recurrence.[2] Most synthetic meshes are made of polypropylene fibers woven or knitted together into sheets. Synthetic polypropylene meshes are highly variable across numerous parameters: pore size, coatings, fiber diameter, and method of construction.[1]

4.1.2 Mesh Characteristics

The material composition of mesh influences its integration into the body. Meshes must be sufficiently strong not to fail and sufficiently elastic to withstand deformation and changes in pressure. Consideration of the mesh pore size is also important; microporous meshes, for example, have smaller pores and are rejected by the host body more frequently, and are associated with chronic inflammation and infection. Scar tissue easily fills the small pores and prevents complete integration of the implant. Macroporous meshes, on the other hand, allow infiltration of immune cells into the mesh, which prevents the formation of bacterial colonies. New connective tissue grows more easily in larger pores and results in more complete mesh integration.

Meshes may be made of monofilament (single strands woven or knitted together) or multifilament (twisted strands woven or knitted together) materials (see Figure 1). Monofilament meshes are stronger, but stiffer. Multifilament meshes are soft, but may host bacterial colonies and erode easily, thereby increasing risk of infection.[2] Mesh erosion may present months or years after mesh implantation, making it difficult to study in short-term trials. Erosion may require mesh excision, which is a difficult procedure and may not resolve symptoms caused by erosion.

Figure 1: Mesh Materials



4.2 Inguinal Hernia

A hernia occurs when an parts of an internal organ protrude through the body wall.[3] The term "hernia" includes a hernia sac, a tissue sac that contains the herniated organ, the sac coverings, and the sac contents. The sac has a neck that extends out of the abdomen. Intestines are the most common sac contents.[4] There are numerous types of hernia, classified based on the location of the herniation. Diaphragmatic, abdominal, femoral, perineal, and lumbar hernias are a few examples of hernia types. The scope of this HTA includes only inguinal hernias, which is a common form of abdominal hernia occurring in the groin.

Inguinal hernia is a common condition, more common in men than women. In men, the lifetime risk of inguinal hernia is 27%, whereas in women the lifetime risk is 3%.[5] Inguinal hernia repair is one of the most common operation in general surgery.[4,5,3] Risk factors for developing inguinal hernia include genetic factors such as tissue abnormalities, mechanical factors such as chronic cough or obesity, and metabolic factors such as collagen instability.[4]

Inguinal hernias may be indirect or direct, depending on whether they pass through the inguinal canal or protrude through the abdominal wall directly. The inguinal canal is a passage approximately 4 cm in length that allows for the passage of structures from inside to outside the abdominal cavity. In male anatomy, the spermatic cord passes through the inguinal canal; in

female anatomy, the round ligament of the uterus passes through the inguinal canal.[6] Indirect inguinal hernias protrude through the deep inguinal ring, the entrance to the inguinal canal. Direct inguinal hernias occur when the hernia protrudes through a weak point in the abdominal wall, not through the inguinal canal.[3] The clinical relevance of the classification of hernias as direct or indirect is considered dated,[5] but the many authors in the literature still classify hernias as direct or indirect.

The primary symptom of inguinal hernia is a lump in the groin. The lump may be painful or not. Diagnosis is most often made by clinical examination, though occasionally ultrasound or rarely MRI may be used.[4] If the hernia can be pushed back into the body cavity with minimal pressure, and appears intermittently, it is considered reducible. Hernias are considered irreducible or incarcerated when the hernia is trapped in place, and cannot be pushed back behind the body wall. Incarcerated hernias are at risk for strangulation, which occurs when blood and lymph flow to the herniation is cut off; it is a serious emergency condition.[3,7] Common causes of incarceration include a tight hernia sac, adhesions between the hernia contents and the sac, and bowel impaction.[7]

Multiple classification schemes exist to categorize inguinal hernias, dating back to 1959. In 2007, the European Hernia Society (EHS) published a classification system that remains the predominant scheme in use.[8,9] This system classifies hernia based on their anatomic location and size. The anatomic location of the hernia is described as type M (medial or direct), L (lateral or indirect), and F (femoral or crural). In terms of size, the EHS system classifies hernias as type 1 (smaller than or equal to the width of the index finger), type 2 (width between one and two fingers), or type 3 (width of three or more fingers). The EHS system may be used to classify hernias either by laparoscopic or open approaches (see Figure 2, Figure 3)

Figure 2: EHS Classification by Laparoscopic Approach

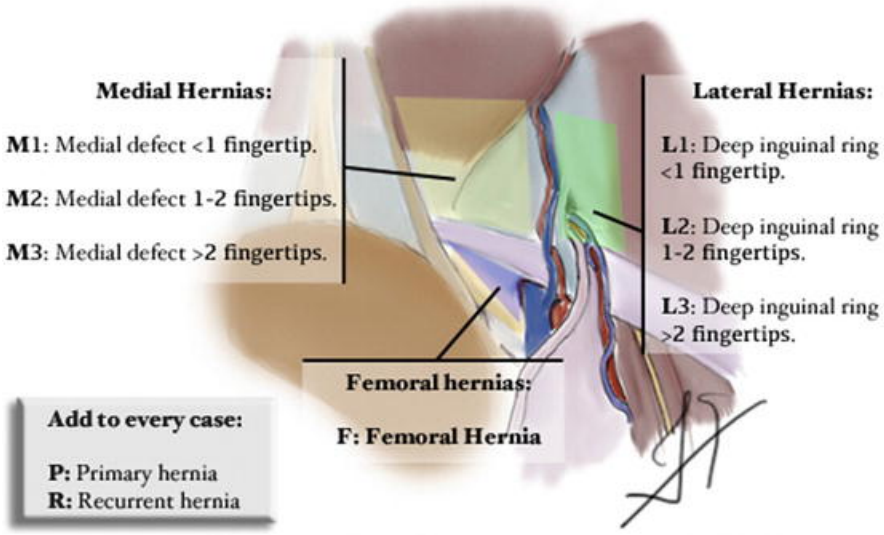
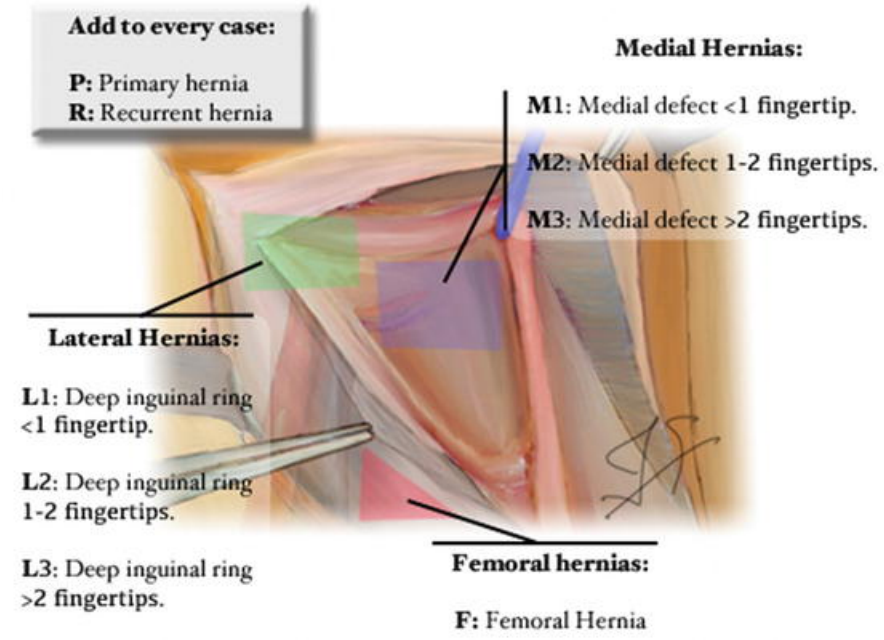


Figure 3: EHS Classification by Open Approach



4.2.1 Treatment of Inguinal Hernia

Hernias of all types are commonly treated with surgery.[3] In complicated or emergency cases, surgery may be required immediately. In uncomplicated symptomatic cases, elective hernia repair may be undertaken. Asymptomatic hernias may go untreated, but caution is warranted; the probability of developing pain, incarceration, and strangulation increases significantly over

time.[3] Operation is indicated for pediatric patients, hernias with narrow sac neck, incarcerated hernia, painful hernia, and obstructed or strangulated hernia. Obstructed hernias should be operated either immediately or within days, and a strangulated hernia should be operated immediately.[4]

Surgery for inguinal hernia repair may or may not involve the use of a mesh implant. Tissue repairs do not use a mesh implant, but typically suture the tissues in place to approximate non-herniated anatomy. Tissue repairs are usually performed with open approaches and include Shouldice, Bassini, or McVay repairs, of which Shouldice is the predominant technique. Mesh repairs may be performed either by open approach or by laparoscopy. Open mesh repair techniques include Lichtenstein, plug repair, or Kugel repair, of which Lichtenstein is the most common. The Lichtenstein technique involves reinforcing the floor of the inguinal canal with a mesh, allowing the spermatic cord (in male anatomy) to pass through a slit in the mesh.[10] Laparoscopic mesh repair may be done by the totally extraperitoneal technique (TEP) or the transabdominal peritoneal patch technique (TAPP).[3] The use of mesh is the gold standard for hernia repair, although the appropriate technique for implantation remains undecided and may vary between cases.[11] In 2017 in the USA, 70% of hernia repairs made use of mesh products.[12]

Table 1: Comparison of Selected Surgical Techniques (adapted from Montgomery[4])

	Shouldice	**Lichtenstein**	**Plug**	**Laparoscopic**
Performed with local anesthesia?	✓	✓	✓	
Short learning curve?		✓	✓	
Use of mesh?		✓	✓	✓
Short operative time?		✓	✓	
Low post-operative pain?				✓
Short return to activity?				✓
Less late discomfort?	✓		*	✓

*unknown- little data

Before 1958, hernias were repaired by approximating normal anatomy and suturing the tissues in place with tension; the technique was pioneered by Bassini in 1884, and remains in use today

(though not as the most common technique).[11] The tension of the sutures is a common reason for repair failure and recurrence. In 1958, Dr. Usher introduced "tension-free" methods of repair with polypropylene mesh, which later evolved into the Lichtenstein technique for mesh implantation.

The first generation of meshes were strong and thick, and designed to induce a fibrotic reaction in the patient's body (Table 2). Fibrosis of the mesh was thought to integrate and reinforce the repair, but led instead to pain and restriction of movement. Lighter weight meshes have decreased tensile strength, but still more than enough strength to withstand abdominal pressure. While lightweight meshes are more flexible, less prone to shrinkage, and cause less pain, they may be associated with infection and recurrence. More research comparing heavyweight and lightweight meshes is required.[3]

Meshes may also be composite, or biological. Composite meshes have a dissolvable component and a permanent component, but their clinical features have yet to be determined. Biological materials such as acellular collagen provide strength while the patient's body incorporates and remodels the new tissue, but the strength of these meshes rapidly degrades *in vivo*.[3]

Table 2: Mesh Types (adapted from Pickett[11])

Mesh	**Advantages**	**Disadvantages**
Heavyweight	Safe, well-studied	More acute pain, possibly more chronic pain
Lightweight	Less acute pain, possibly less chronic pain	
Semi-absorbable	No apparent difference from totally permanent mesh	Increased cost
Collagen	Can be placed in patients at risk for infection	Increased cost Sparse long-term data

5 Environmental Scan of Advisories and Licenses

Summary:

- Many inguinal hernia meshes are available for implantation in Canada and the United States.
- No broad actions against the use of mesh for inguinal hernia repair have been taken by the countries included in this analysis; however, certain products have been banned in Canada and the United States.
- The new Action Plan on medical devices published by Health Canada in 2018 will intensify the pre-market approval process, increase post-market surveillance, and enhance the transparency of approval and surveillance of medical devices, including surgical synthetic mesh for inguinal hernia repair.

5.1 Purpose

An environmental scan was conducted to determine status and licensure of surgical meshes for inguinal hernia repair in Canada and internationally.

5.2 Methods

The Canadian Medical Devices Active License Listing was searched for mesh products licensed in Canada. The Government of Canada's Recalls and Safety Alerts was searched for mesh-related advisories and recalls. Health Canada was contacted to request a list of mesh products available in Canada. A search of health advisory agencies in the United States, Australia, New Zealand, and the UK was also conducted to characterize these countries' stances on hernia mesh products.

5.3 Findings

5.3.1 Meshes Available in Canada

Canadian law, specifically the Medical Devices Regulations (SOR/98-282), classifies medical devices according to their risk. Class I devices are associated with the smallest risk, and class IV devices are associated with the highest risk (Table 3).[13] Most surgical meshes licensed in Canada are class III: they are invasive devices that remain in the body for more than 30 days (see Table 4). While some individual meshes have been removed from the market in Canada (see Table 5) no broad recalls have been issued. Table 4 shows a selection of permanent, semi-permanent, and dissolvable hernia meshes currently available in Canada.

Table 3: Canadian Medical Device Classes (Invasive Devices) [13]

Class	Risk	Description of Devices in Class	Examples
Class I	Lowest	Invasive devices that are placed in oral or nasal cavities	Manual toothbrush, dressing for nosebleed
Class II	Low-moderate	Invasive devices that penetrate the body through an orifice or contact the surface of the eye (rule 2; subrule 1)	Contact lenses, urethral catheter
Class III	High-moderate	Invasive devices that remain in the body for 30 or more consecutive days, or is intended to be absorbed by the body (rule 2; subrule 3)	Intrauterine contraceptive device, ureteral stent
Class IV	Highest	Any device made from or incorporating human or animal tissues or tissue derivatives (rule 14; subrule 1)	Porcine heart valve, bone graft

Table 4: Selection of Surgical Meshes Available in Canada

Class	Company name	Mesh name	Date approved
3	Davol Inc.	Bard Mesh Dart and Plug	2013-05-31
		Kugel Hernia Patch	2013-05-31
		Ventralex Hernia Patch	2018-06-22
		Bard Modified Kugel Hernia Patch	2013-05-31
		Bard PolySoft Hernia Patch	2013-05-31
		Ventrio Hernia Patch	2018-16-22
	Ethicon	Prolene Polypropylene Mesh	2017-11-20
	Johnson & Johnson International	UltraPro Mesh	2016-09-30
		UltraPro Plug Device	2013-05-13
		UltraPro Hernia System	2013-05-13
		Proceed Ventral Patch	2013-05-13
	Sofradim Production	Parietene Mesh	2018-10-09
		Parietex Hyrophilic Mesh	2018-10-23

		ProGrip Self-Gripping Polypropylene Mesh	2018-10-09
	Insightra Medical	Freedom Ventral Hernia Repair System	2017-12-27
	Atrium Medical Corporation	Atrium Surgical Mesh (Prolite, Proloop)	2018-04-18
4	Sofradim Production	Parietene Composite Mesh	2014-11-26
		Parietex Composite Mesh Polyester with Absorbable Collagen Film	2018-06-15
		Parietex Plug and Patch System	2018-10-09
		Symbotex Composite Mesh	2018-06-15

5.3.2 Advisories and Withdrawals from the Market

No broad actions against hernia meshes have been taken in Canada and internationally; however, several products have been recalled in Canada and the US since 2006 due to safety concerns (see publicly available information on specific surgical mesh product recalls in Table 5; no information was available regarding recall of hernia meshes in Australia, New Zealand, and the UK). Significant concern has arisen in recent years over the use of surgical mesh for pelvic organ prolapse and stress urinary incontinence. Several countries have issued statements of concern or bans on meshes for these purposes. The meshes used to treat these urogynaecological conditions are similar to the meshes used to treat inguinal hernia, but there is significantly less concern regarding hernia meshes because hernia mesh implantation results in different complications and complication rates.[14]

Table 5: Publicly Available Information on Specific Hernia Mesh Product Recalls in Canada and the Internationally

Country	**Manufacturer/Product**	**Recall Date**
Canada	Ethicon: Physiomesh Flexible composite Mesh (global recall)[15]	May 25, 2016
	Ethicon: Proceed Surgical Mesh	Feb 2014[16], Jan 2006[17]
	Coated C-Qur Meshes[18]	Jul 2013
	Bard Composix Kugel Mesh X-Large Patch[19]	Jan 2006

	Ventralight ST Mesh with Echo[20]	Apr 2014
US	C.R. Bard/Davol Flat Mesh (2" x 4", 10" x 14", 3" x 6", 6" x 6") (counterfeit mesh)[21]	Jun 2, 2010
	Ethicon: Physiomesh Flexible composite Mesh (global recall)	May 2016
	Ethicon: Proceed Surgical Mesh[22]	Apr 2014
UK	--	--
New Zealand	--	--
Australia	--	--

In December 2018, Health Canada published an Action Plan to intensify the pre-market approval process, increase post-market surveillance, and enhance the transparency of approval and surveillance of medical devices, including surgical synthetic mesh for inguinal hernia repair. To strengthen the pre-market approval process, starting in early 2019 Health Canada plans to allow medical professionals to apply to conduct investigations into medical devices (where before only manufacturers are able to do so). Health Canada will also review its evidence requirements for approval of high-risk medical devices.[23] This process should decrease the number of defective surgical mesh devices for inguinal hernia repair that enter the Canadian market.

To increase the robustness of post-market surveillance, *Vanessa's Law* will require Canadian hospitals to report medical device complications, which will include complications of inguinal hernia mesh surgeries. Health Canada will also expand the Canadian Medical Devices Sentinel Network. *Vanessa's Law* will also obligate manufacturers to provide more information to Health Canada, such as notifying Health Canada of regulatory actions taken by foreign regulatory agencies, and it will allow Health Canada to require manufacturers to undertake additional studies on devices. The *Regulatory Review of the Drugs and Devices initiative* will propose a framework to increase the use of real world evidence to evaluate devices throughout their market lifespans. Lastly, more inspectors, more frequent inspections, onsite inspections of foreign manufacturers, and rigorous investigations will also support post-market surveillance.[23] Increased attention paid to post-market surveillance will be a particularly crucial point for inguinal hernia repair with mesh, for which complications can arise several years after the surgery.

To improve transparency, Health Canada will begin to release the evidence upon which it bases its approvals. In January 2019, Health Canada will publish summaries of its decisions for class

III devices (where before only class IV device reports were published). A searchable database will be launched to allow Canadians to access device incident reports, and Health Canada's inspection results and regulatory actions.[23]

5.3.3 Class-action Lawsuits in Canada and the United States

Several Canadian class action lawsuits and a mass tort lawsuit have been launched against hernia mesh manufacturers, including inguinal mesh. Affected companies include Ethicon, Bard Davol, Atrium Medical, Medtronic, Johnson & Johnson, American Medical Systems, and Boston Scientific. The class-action lawsuits have been launched by the Consumer Law Group[24] and Siskinds LLP[25] and allege that the mesh manufacturers failed to adequately warn patients that using certain hernia mesh products increases the risk of serious injuries and complications. The hernia mass tort lawsuit was launched by Howie, Sacks and Henry LLP and is representing patients who have had mesh implant complications, infection recurrence, recognizing that the extent of the injuries from the mesh products varies across patients.[26] At this time, there are no class action suits against hernia mesh manufacturers in the United States.[27]

5.4 Conclusions

While complications of surgical mesh for POP and SUI have raised significant alarm over the use of surgical mesh, mesh for hernia repair has not been subject to broad regulatory bans in any country studied. Some individual meshes have been withdrawn from the market due to safety concerns, and several lawsuits have been launched against mesh manufacturers. In Canada, recent and planned actions to improve the safety of medical devices in general are expected to affect future hernia mesh repair.

6 Review of Guidelines and Best Practice Recommendations

Summary:

- For repair of inguinal hernia, the HerniaSure Group and BHS both recommend the use of surgical mesh, particularly using a laparoscopic/laparo-endoscopic technique.
- TAPP and TEP are generally regarded as having comparable patient outcomes and the choice of technique should be based on the surgeon's expertise.
- Recommendations from the HerniaSurge Group regarding mesh material use include not selecting mesh solely based on terms "lightweight" or "heavyweight" and not using three-dimensional implants (plug-and-patch bilayer).

6.1 Purpose

To synthesize current guidelines and best practice recommendations on the use of surgical mesh for inguinal hernia.

6.1 Methods

A grey literature search was conducted. CADTH's *Grey Matters* guide was used to locate agencies issuing guidelines. Searches were conducted on the websites of these agencies for guidelines related to surgical mesh specifically and surgical management of inguinal hernia generally. A review of the guidelines was conducted to eliminate those guidelines that covered inguinal hernia treatment but did not address mesh technologies.

6.2 Results

Two relevant guidelines were identified (see Table 6): the HerniaSurge Group guideline published in 2018[8] and the British Hernia Society (BHS) guideline published in 2013.[28] The HerniaSurge Group guideline was published by an international coalition of experts and surgeons and has been endorsed by hernia organizations such as the European Hernia Society (EHS) and the International Endohernia Society (IEHS). Therefore treatment guidelines published by EHS and IEHS were considered outdated and are therefore not reported here. We chose to report the BHS guidelines because it was unclear from their website whether they endorse the guidelines published by the HerniaSurge Group; however, it should be noted that the BHS guidelines were published in 2013 and may be outdated.

Surgical mesh is considered a standard treatment for inguinal hernia, and both guideline recommendations focus largely on choice of technique for different populations and hernia types (e.g., bilateral, recurrent), as well as choice of mesh materials. Key recommendations are summarized below, with full recommendations regarding mesh use summarized in Table 6. Both guidelines recommend surgical mesh for treatment of inguinal hernia.[8,28]

With respect to laparo-endoscopic technique, both guidelines suggest that TAPP and TEP have comparable patient outcomes, and the HerniaSurge Group recommends basing the choice of technique on the surgeon's expertise. With some exceptions, the HerniaSurge Group recommends the laparo-endoscopic technique as the treatment for male patients with primary unilateral inguinal hernia and laparo-endoscopic repair with mesh implementation (provided expertise is available) as the treatment for groin hernias in women.[8] For bilateral hernia, the HerniaSurge Group recommends laparo-endoscopic repair,[8] and BHS recommends laparoscopic repair.[28]

For recurrent inguinal hernias, the HerniaSurge Group recommends laparo-endoscopic repair in cases of failed anterior tissue or Lichtenstein repair.[8] BHS guideline suggests that the technique used in the original hernia repair should be taken into consideration when selecting a technique for repair of recurrence, such that if the initial repair operation was laparoscopic, then the recurrent operation should be open anterior repair, and vice versa.[28]

Both guidelines make several recommendations regarding mesh types and materials to be used for inguinal hernia repair. Notably, the HerniaSurge Group strongly recommends not selecting mesh solely based on terms "lightweight" or "heavyweight", until clear definitions of those terms are developed. The HerniaSurge Group also strongly recommends against the use of three-dimensional implants (plug-and-patch bilayer), despite comparable results. BHS guideline suggests that all inguinal hernias be repaired using flat mesh, and that there is no clinical advantage of plugs vs. flat mesh for open inguinal repair. BHS also suggests that "light-weight" (large pore) mesh should be used.

6.3 Conclusions

The HerniaSure Group and BHS both recommend surgical mesh, particularly using a laparoscopic/laparo-endoscopic technique, for inguinal hernia repair. The two guidelines largely focused their recommendations on choice of technique for different populations and inguinal hernia types, as well as choice of mesh. With respect to technique, TAPP and TEP are generally regarded as having comparable patient outcomes and the technique choice should be based on the surgeon's expertise. Recommendations from the HerniaSurge Group regarding mesh material use include not selecting mesh solely based on terms "lightweight" or "heavyweight" and not using three-dimensional implants (plug-and-patch bilayer).

Table 6: Guidelines on the Use of Surgical Meshes for Inguinal Hernia

Organization, year, country	Type of publication	Title	Condition, device	Recommendations
The Hernia Surge Group[8] 2018 Netherlands Funding Source: grants through Bard and Johnson & Johnson	Management guidelines	International guidelines for groin hernia management	Inguinal hernia, mesh devices	• A mesh-based repair technique is recommended for patients with inguinal hernias (evidence: moderate; recommendation: strong, upgraded). • The use of open pre-peritoneal mesh techniques to replace the standard flat mesh in the Lichtenstein technique is suggested to be performed in research settings (evidence: very low; recommendation: weak). • In laparo-endoscopic inguinal hernia repair, as TAPP and TEP have comparable outcomes, it is recommended that the choice of the technique be based on the surgeon's skills, education, and experience (evidence: moderate; recommendation: strong, upgraded). • For male patients with primary unilateral inguinal hernia, a laparo-endoscopic technique is suggested because of a lower postoperative pain incidence and a reduction in chronic pain incidence, provided that a surgeon with specific expertise and sufficient resources is available. However, there are patient and hernia characteristics that warrant Lichtenstein as first choice (evidence: moderate; recommendation: weak downgraded). Bilateral hernia • Laparo-endoscopic repair is recommended for the repair of primary bilateral inguinal hernias provided that a surgeon with specific expertise and

Organization, year, country	Type of publication	Title	Condition, device	Recommendations
				sufficient resources is available (evidence: low; recommendation: strong, upgraded). Mesh fixation • Atraumatic mesh fixation in open inguinal hernia repair techniques is suggested to reduce early postoperative pain (evidence: very low; recommendation: very weak). • Mesh fixation is recommended in patients with large direct hernias (M3-EHS classification) undergoing TAPP or TEP to reduce recurrence risk (evidence: very low; recommendation: strong, upgraded). • Mesh fixation to the pubic bone is not recommended since this leads to an increased incidence of chronic pain (evidence: low; recommendation: strong, upgraded). Groin hernias in women • Provided expertise is available, women with groin hernias are recommended to undergo laparo-endoscopic repair with mesh implementation (evidence: moderate; recommendation: strong, upgraded). Recurrence after anterior repair • Laparo-endoscopic recurrent inguinal hernia repair is recommended after failed anterior tissue or

Organization, year, country	Type of publication	Title	Condition, device	Recommendations
				Lichtenstein repair (evidence: low; recommendation: strong, upgraded). Mesh types and materials • Despite comparable results, three-dimensional implants (plug-and-patch bilayer) are not recommended because of the excessive use of foreign material, the need to enter both the anterior and posterior planes and the additional cost (evidence: moderate; recommendation: strong, upgraded). • The use of other implants to replace the standard flat mesh in the Lichtenstein technique is currently not recommended (evidence: moderate; recommendation: strong, upgraded). • Before a clear definition of LWM and HWM is developed, the selection of mesh based solely on the terms “lightweight” or “heavyweight” is not recommended (evidence: low; recommendation: strong, upgraded). • HerniaSurge suggests large pore (1-1.5mm) monofilament synthetic flat meshes with a burst strength of 16 N/m^2 and consisting of a minimum tensile strength in all directions (including subsequent tearing force) of 16 N/m^2 (evidence: low; recommendation: weak). • When considering postoperative pain after inguinal hernia repair, it is suggested to consider a so-called LWM, although probably these are only

Organization, year, country	Type of publication	Title	Condition, device	Recommendations
				short-term benefits (evidence: low; recommendation: weak).
British Hernia Society[28] 2013 UK Funding Source: Not Reported	Management guidelines	Groin Hernia Guidelines	Inguinal hernia, prosthetic meshes	TEP vs TAPP • There is no evidence supporting TEP ahead of TAPP or vice versa. (Grade C) • TAPP may be beneficial if there is diagnostic uncertainty in cases of groin/lower abdominal pain, since it can be used to grossly assess intra-abdominal structures. (Grade D; Good Practice Point [GPP]) Mesh materials • All adult inguinal hernias should be repaired using flat mesh (or non-mesh Shouldice repair, if experience is available). (Grade A) • There is no clinical advantage of plugs compared with flat mesh for open inguinal hernia repair. (Grade A) • A cost-effective 'lightweight' (large pore) mesh should be used. (Grade A) • The use of a large mesh for laparoscopic inguinal hernia repair is supported by the literature, albeit with a low level of evidence, which makes it impossible to recommend an optimal size. However, it seems reasonable to suggest that the mesh should overlap the hernia defect by at least 3 cm in all directions, and we recommend a mesh of at least 15 x 10 cm. It should be emphasized that, in laparoscopic repair, dissection of the

Organization, year, country	Type of publication	Title	Condition, device	Recommendations
				preperitoneal space has to be adequate for the size of mesh, to ensure that the mesh lies flat against the abdominal wall. (Grade B) Groin hernias in women • Groin hernias in women should be repaired laparoscopically. (Grade B) Recurrent groin hernias • The technique used in the index hernia repair should be taken into account when choosing the technique for repair of recurrence. If the initial approach was an open anterior repair, then the recurrent operation should be a laparoscopic repair and vice versa. (Grade B) • There is no evidence to promote one laparoscopic approach ahead of another (TEP or TAPP), and the choice should be dependent on surgeon expertise and preference. (Grade B) • Open anterior repair is recommended in patients who received primary repairs that place mesh in the preperitoneal space (e.g., Kugel patch, Prolene Hernia System, and plugs) and patients who have had previous preperitoneal dissection, such as for a prostatectomy, or operations involving the iliac vessels or a preperitoneally located transplanted kidney. (Grade C) • Patients with severe cardiac or pulmonary diseases may be better treated with open repair with local

Organization, year, country	Type of publication	Title	Condition, device	Recommendations
				anesthesia, and open preperitoneal repair should be considered. (Grade C) • Patients who are anticoagulated or are at risk for bleeding may be better suited to open repair. (Grade D; GPP) • Recurrent hernias in women should be repaired laparoscopically because the repair may represent a femoral hernia. (Grade D; GPP) Bilateral groin hernias • Bilateral inguinal hernias should be repaired laparoscopically from a cost-utility and patient perspective. (Grade D; GPP) • Current evidence does not show significant difference in outcomes after open versus laparoscopic repair of bilateral inguinal hernias. (Grade B)

7 Review of Health Technology Assessments

Summary

- Two inguinal hernia HTAs were identified; one HTA found that open preperitoneal mesh repair was more clinically effective than Lichtenstein mesh repair; the other HTA found that laparoscopic repair was more clinically effective than open mesh repair.
- Specific recommendations regarding the use of surgical mesh for inguinal hernia were not provided; additional research is warranted.

7.1 Purpose

To synthesize health technology assessments (HTAs) on synthetic surgical mesh for treatment of inguinal hernia.

7.2 Methods

7.2.1 Search Strategy

A grey literature search was conducted, guided by the Canadian Agency for Drugs and Technologies in Health's (CADTH) "Grey Matters" document. In addition, grey literature and the websites of known HTA organizations were searched using terms including "surgical mesh," "polypropylene mesh," "surgical mesh inguinal hernia," "surgical hernia repair," and most broadly, "mesh." The grey literature search was conducted on January 3, 2019 and updated on February 8, 2019.

7.2.2 Study Selection

The database search did not identify any relevant HTA publications on synthetic surgical mesh for inguinal hernia that had not already been identified by the grey literature search. HTAs and evidence reviews retrieved from the grey literature search were screened in duplicate and were included in the review if they met all inclusion criteria and failed to meet any exclusion criteria in Table 7. Only HTA publications with a full systematic review of clinical effectiveness of any of the technologies of interest were included. Any discrepancies between reviewers' inclusions were resolved through discussion between the reviewers.

Table 7: Inclusion and Exclusion criteria for HTA Review

Inclusion Criteria	Exclusion Criteria
• HTA or evidence review on surgical mesh for inguinal hernia • Adult population • English or French Language only	• Not an HTA or evidence review • Not synthetic surgical mesh • Not available in English or French • Full text not available

Abbreviations: HTA: health technology assessment

7.2.3 Data Extraction

Data from the included HTAs were extracted in duplicate. Extracted outcomes included: study characteristics (author/date, country, study objectives, data collection methods, amount and type of evidence included), details on clinical effectiveness, cost-effectiveness and any *de novo* models included in each HTA, and recommendations. Discrepancies between reviewers during data extraction were resolved through discussion.

7.3 Results

The grey literature search identified two HTAs for inguinal hernia.[29,30] No additional records were identified through the HTA database search. Findings from the HTAs included in this review are synthesized below.

7.3.1 Study Characteristics

Two inguinal hernia HTAs were included in this review; both of them were published in the UK.[29,30] Both of them conducted clinical and cost-effectiveness reviews, as well as cost-effectiveness analyses using a Markov models.[29,30] The UK National Institute for Health Research (NIHR) HTA was conducted in 2015 and compared open preperitoneal mesh repair with standard Lichtenstein mesh repair.[30] The UK NHS HTA was conducted in 2005 and compared open mesh repair to laparoscopic surgery (TAPP vs TEP).[29] A detailed summary of study characteristics is presented in Table 8 below.

7.3.2 Clinical Effectiveness Findings

The main outcomes assessed in the inguinal hernia HTAs were patient-reported outcomes (e.g., pain, QoL), as well as clinical and surgical outcomes (e.g., complications, recurrence); see Table 9.[29,30] The UK NIHR HTA found that open preperitoneal mesh repair was associated with less

pain and numbness, fewer recurrences, and fewer complications than Lichtenstein mesh repair.[30] The UK NHS HTA found that laparoscopic repair was associated with less persisting pain and numbness, as well as a faster return to usual activities than open mesh repair; however, it was also associated with a higher rate of serious complications related to visceral injuries (particularly bladder injuries) and longer operation times.[29]

7.3.3 Cost-Effectiveness Findings

Both of the inguinal hernia HTAs conducted reviews of cost-effectiveness (see Table 10).[29,30] The UK NIHR HTA found evidence that the quality-adjusted life-weeks difference for transinguinal preperitoneal (TIPP) versus Lichtenstein mesh repair was 0.00983 (95% CI – 1.01250 to 1.03217). Their own model found that the open preperitoneal procedure was the most efficient and dominant treatment strategy with a high (> 98%) probability of being cost-effectiveness for the NHS at a willingness to pay of £20,000 for a QALY.[30] The NHS UK HTA found evidence that laparoscopic repair was more costly than open mesh in all but two of the 14 studies identified by their systematic review. Their own model analysis found that the mean incremental cost per QALY for TEP compared with open mesh is less than £10,000 and there is approximately an 80% chance that TEP is the most cost-effective intervention should society's maximum willingness to pay for an additional QALY be £20,000.[29]

7.4 Conclusion

Two inguinal hernia HTAs were identified in this review, and both evaluated clinical effectiveness and cost-effectiveness. One inguinal hernia HTA favoured open preperitoneal mesh repair over Lichtenstein mesh repair; the other HTA favoured laparoscopic over open mesh repair. Model analysis in the UK NIHR HTA found that open preperitoneal procedure was the most efficient and dominant treatment strategy over Lichtenstein repair. Model analysis in the NHS UK HTA found that laparoscopic surgery (TEP) was likely more cost-effective than open mesh repair.

Neither of the HTAs provide any specific recommendations for or against the use of surgical mesh. Rather, both outline the need for additional research on these devices using methodologically sound RCTs (see Table 11).

Table 8: Characteristics of Included HTA Publications

Device	Organization, Country	Year	Research Question	Clinical Effectiveness	Cost Effectiveness	Economic Model
Open preperitoneal mesh repair vs standard Lichtenstein mesh repair	National Institute for Health Research (NIHR), Health Technology Assessment programme, UK	2015	"determine the clinical effectiveness and cost-effectiveness of open preperitoneal mesh repair compared with Lichtenstein mesh repair in adults presenting with a clinically diagnosed primary unilateral inguinal hernia"	**Databases**: MEDLINE, MEDLINE In-Process & Other Non-Indexed Citations, EMBASE, Bioscience Information Service, Science Citation Index, Scopus Articles In Press, Cochrane Central Register of Controlled Trials, the Cochrane Database of Systematic Reviews, DARE, and the HTA Database **Search dates**: inception to 31 October/ 1 November 2014 **Primary outcomes:** patient-reported outcomes (e.g., chronic pain, QoL), clinical and surgical outcomes (e.g., complications, recurrence)	**Databases**: NHS EED, HTA Database, MEDLINE, MEDLINE In-Process & Other Non-Indexed Citations, EMBASE, Research Papers in Economics, Science Citation Index, and the Cost-effectiveness Analysis Registry **Search dates**: inception to 31 October/ 1 November 2014 / 3 November 2014 **Primary outcomes:** costs	Markov model for open mesh procedures

Laparoscopic surgery (TAPP vs TEP) vs open mesh repair	NHS R&D HTA Programme, UK	2005	"determine whether laparoscopic methods are more effective and cost-effective than open mesh methods of inguinal hernia repair, and then whether laparoscopic TAPP repair is more effective and cost-effective than laparoscopic TEP"	**Databases**: MEDLINE, MEDLINE Extra, EMBASE, CIHAIL, BIOSSIS, Science Citation Index, Web of Science Proceedings, Cochrane Controlled Trials Register, Cochrane Database of Systematic Reviews, DARE, HTA Database, Journal@Ovid Full Text, SpringerLink, National Research Register, Clinical Trials, Current Controlled Trials, Research Findings Register **Search dates**: 2000-2003 for MEDLINE and EMBASE; June 2003 for others **Primary outcomes:** hernia recurrence, persisting pain	**Databases**: MEDLINE, MEDLINE Extra, EMBASE, NHS EED Database, HMIC, Journals@Ovid Full Text **Search dates**: 2000-2003 for MEDLINE and EMBASE; July 2003 for others **Primary outcomes:** costs	Markov model

Abbreviations: CUA: cost-utility analysis; HTA: health technology assessment; NHS: National Health Service; QoL: quality of life; R&D: research and development; TAPP: transabdominal preperitoneal; TEP: totally extraperitoneal; UK: United Kingdom

Table 9: Clinical Effectiveness and Safety Findings from Included HTA Publications

Device	Organization, Country, Year	Evidence Identified	Findings	Conclusions
Open peritoneal mesh repair vs standard Lichtenstein mesh repair	NIHR, UK, 2015	**12 RCTs**	• Participants who underwent open preperitoneal mesh repair returned to work and normal activities significantly earlier than those who underwent Lichtenstein mesh repair [mean difference –1.49 days, 95% CI –2.78 to –0.20 days]. • Although no significant differences were observed between the two open approaches for incidence of pain [RR 0.50, 95% CI 0.20 to 1.27], numbness (RR 0.48, 95% CI 0.15 to 1.56), recurrences (Peto odds ratio 0.76, 95% CI 0.38 to 1.52) or postoperative complications, fewer events were generally reported after open preperitoneal mesh repair.	• In general, patients randomized to open preperitoneal mesh repair showed lower incidence of pain and numbness, fewer recurrences and fewer complications than those randomized to Lichtenstein mesh repair; however, CIs for treatment effects were wide and most results were not statistically significant at the conventional 5% level.
Laparoscopic surgery (TAPP vs TEP) vs open mesh repair	NHS, UK, 2005	**37 RCTs/quasi-RCTs** (TAPP vs open flat mesh, n=13; TAPP vs open preperitoneal mesh, n=4; TAPP vs plug and mesh**,** n=1; TEP vs open flat mesh, n=7;	**TAPP vs TEP** • Only one small RCT met inclusion criteria; no differences were found between TAPP and TEP in terms of length of operation, haematomas, time to return to usual activities and hernia recurrence, but the CIs were all wide.	• Laparoscopic repair is associated with a faster return to usual activities and less persisting pain and numbness. There also appear to be fewer cases of wound/superficial infection and haematoma. However, operation times are longer and there appears to be a

		TEP vs open preperitoneal mesh, n=5; TEP vs plug and mesh, n=1; TEP vs open flat mesh vs open preperitoneal mesh, n=1; TEP vs open flat mesh vs plug and mesh, n=1; mixed laparoscopic vs mixed open, n=2; mixed laparoscopic vs open flat mesh, n=1; and TAPP vs TEP, n=1)	**TAPP vs TEP vs open mesh** • For bilateral hernias, there was a scarcity of data. When considering the TEP groups, the duration of operation was longer than the open mesh groups (p = 0.04). However, when considering the TAPP method of repair for bilateral hernias, the duration of operation appeared to be similar to that of the open mesh groups (p = 0.9). • There is also statistically significant evidence to suggest that following a TAPP repair there are fewer cases of wound/superficial infection and persisting numbness and that time to return to usual activities is shorter. **TAPP vs open mesh** • Recurrent hernias: no difference between the groups with respect to persisting pain and hernia recurrence (RR 1.0, 95% CI 0.54 to 1.85, p = 1, and RR 1.32, 95% CI 0.53 to 3.31, p = 0.5, respectively). • Bilateral hernias: no difference between the groups when comparing persisting pain and hernia recurrence (RR 0.8, 95% CI 0.45 to 1.45, *p* = 0.5; and RR 2.02, 95% CI 0.52 to 7.83, *p* = 0.3, respectively).	higher rate of serious complications in respect of visceral (especially bladder) injuries. • Mesh infection is very uncommon with similar rates noted between the surgical approaches. There is no apparent difference in the rate of hernia recurrence. • Very limited data were available about rare complications and for the subgroup analyses of recurrent and bilateral hernias; although data are presented, these have questionable reliability and hence limited generalizability.

			TEP vs open mesh • Recurrent hernias: no difference in the reported number of cases of persisting numbness, persisting pain and hernia recurrence (RR 1.22, 95% CI 0.63 to 2.35, p = 0.6; RR 0.9, 95% CI 0.59 to 1.38, p = 0.6; and RR 1.08, 95% CI 0.57 to 2.05, p = 0.8, respectively). • Bilateral hernias: no difference in the reported number of cases of persisting numbness, persisting pain and hernia recurrence (RR 1.05, 95% CI 0.49 to 2.22, *p* = 0.9; RR 0.97, 95% CI 0.62 to 1.52, *p* = 0.9; and RR 4.44, 95% CI 0.52 to 38.01, *p* = 0.17, respectively).	

Abbreviations: CI: confidence interval; HTA: health technology assessment; MAS: Medical Advisory Secretariat; National Institute for health Research; QoL: quality of life; RCT: randomized controlled trial; RR: risk ratio; TAPP: transabdominal preperitoneal; TEP: totally extraperitoneal; TIPP: transinguinal preperitoneal; UK: United Kingdom

Table 10: Cost-effectiveness Systematic Review Findings from Included HTA Publications

Device	Organization, Country, Year	Evidence Identified	Findings	Conclusions
Open peritoneal mesh repair vs standard Lichtenstein mesh repair	NIHR, UK, 2015	Systematic review: 1 CEA	**Systematic review**: • Mean quality-adjusted life-weeks difference for TIPP versus Lichtenstein mesh repair was 0.00983 (95% CI –1.01250 to 1.03217). • If the data presented for QoL were combined with the reported cost data, TIPP would, on average, be less costly and more effective than Lichtenstein mesh repair and would thus be the most efficient, dominant treatment strategy. However, such results would be subject to a high degree of uncertainty. **Model**: • Open preperitoneal mesh repair was £256 less costly and improved health outcomes by 0.041 QALYs compared with Lichtenstein mesh repair. • The open preperitoneal procedure was the most efficient and dominant treatment strategy with a high (> 98%) probability of being cost-effectiveness for the NHS at a willingness to pay of £20,000 for a QALY.	• Overall, the results indicate that surgical treatment of primary inguinal hernia repair using open preperitoneal mesh repair surgery is likely to be a highly cost-effective use of NHS resources compared with the standard Lichtenstein mesh repair.

Device	Organization, Country, Year	Evidence Identified	Findings	Conclusions
Laparoscopic surgery (TAPP vs TEP) vs open mesh repair	NHS, UK, 2005	Systematic review: 14 studies included for review of economic evaluations	**Systematic review:** • Laparoscopic repair was more costly than open mesh in all but two of the 14 studies. Laparoscopic repair is more costly to the health service than open repair, with an estimated extra cost from studies conducted in the UK of about £300–350 per patient. The point estimates of cost provided by the economic model also suggest that the laparoscopic techniques are more costly (around £100–200 more per patient after 5 years). **Model:** • Open flat mesh is the least costly option but provides less QALYs than TEP or TAPP. • TEP is likely to dominate TAPP (on average TEP is estimated to be less costly and more effective). • Mean incremental cost per QALY for TEP compared with open mesh is less than £10,000 and there is approximately an 80% chance that TEP is the most cost-effective intervention should society's maximum willingness	• It is likely that, for management of symptomatic bilateral hernias, laparoscopic repair would be more cost-effective as differences in operation time (a key cost driver) may be reduced and differences in convalescence time are more marked (hence QALYs will increase) for laparoscopic compared with open mesh repair. • When possible repair of contralateral occult hernias is taken into account, TEP repair is most likely to be considered cost-effective at threshold values for the cost per additional QALY above £20,000.

Device	Organization, Country, Year	Evidence Identified	Findings	Conclusions
			to pay for an additional QALY be £20,000.	

Abbreviations: BIA: budget impact analysis; CAD: Canadian dollar; CEA: cost-effectiveness analysis; HTA: health technology assessment; MAS: Medical Advisory Secretariat; NIHR: National Institute for health Research; NHS: National Health Service; QALY: quality-adjusted life year; RCT: randomized controlled trial; TAPP: transabdominal preperitoneal; TEP: totally extraperitoneal; TIPP: transinguinal preperitoneal; UK: United Kingdom

Table 11: Recommendations from Included HTA Publications

Device	Organization, Country, Year	Conclusions / Recommendations
Open peritoneal mesh repair vs standard Lichtenstein mesh repair	NIHR, UK, 2015	• Current evidence indicates, although with some uncertainty, that the open preperitoneal approach may be a safe and efficacious alternative to the standard Lichtenstein approach for the treatment of inguinal hernia with similar recurrence and complication rates, potentially lower incidence of postoperative pain, and a significant earlier return to work and to usual daily activities. • A large, well-designed clinical trial comparing the long-term effects of open preperitoneal mesh repair versus standard Lichtenstein mesh repair with regard to chronic pain, complications, recurrences, and cost in people with primary unilateral inguinal hernia is required.
Laparoscopic surgery (TAPP vs TEP) vs open mesh repair	NHS, UK, 2005	• Laparoscopic repair is associated with a faster return to usual activities and less persisting pain and numbness. There also appear to be fewer cases of wound/superficial infection and haematoma. However, operation times are longer and there appears to be a higher rate of serious complications in respect of visceral (especially bladder) injuries. Mesh infection is very uncommon with similar rates noted between the surgical approaches. There is no apparent difference in the rate of hernia recurrence. • More evidence is required on the loss of utility caused by persisting pain and numbness, as well as serious complications resulting from minor surgery; and whether the balance of advantages and disadvantages changes when hernias are recurrent or bilateral. • Questions remain about the relative merits and risks of TAPP and TEP, and methodologically sound RCTs are needed.

Abbreviations: HTA: health technology assessment; MAS: Medical Advisory Secretariat; NIHR: National Institute for health Research; QALY: quality-adjusted life year; RCT: randomized controlled trial; TAPP: transabdominal preperitoneal; TEP: totally extraperitoneal; UK: United Kingdom

8 Systematic Review of Safety and Efficacy of Surgical Mesh for Inguinal Hernia Repair

Summary:

- Twenty unique RCTs and three follow-up studies were identified that evaluated the effectiveness of synthetic surgical mesh for inguinal hernia against comparators of interest.
- Nineteen studies compared synthetic mesh to suture repair and four compared synthetic mesh to porcine mesh.
- A meta-analysis of recurrence rates for synthetic mesh vs. suture repair using risk differences found that that the risk of recurrence at <1 year is 1% greater with synthetic mesh than with suture repair but is 2% smaller at 1-2 years, 3-5 years, and ≥5 years. These effects are not significant and the latter three are associated with moderate-to-substantial heterogeneity and should be interpreted with caution.
- A meta-analysis of recurrence rates for synthetic vs. porcine mesh using risk differences found that the risk of recurrence at 6-12 months is 6% smaller with synthetic mesh than with porcine mesh; however, this effect is not significant.
- Meta-analyses of complications suggest that synthetic mesh is not significantly different from suture repair with respect to risk of infection, pain, hematoma, seroma, testicular atrophy, urinary retention, and neurological complications (all 0-3% differences), and not significantly different from porcine mesh with respect to risk of infection, pain, hematoma, and seroma (all 0-8% differences).

8.1 Purpose

To assess the clinical effectiveness and safety profile of permanent, synthetic surgical mesh for treatment of inguinal hernia in adults.

8.2 Methods

8.2.1 Search Strategy

A systematic review of the literature was completed. MEDLINE, EMBASE, Cochrane Central, and CINAHL were searched from inception. The search was performed on December 20, 2018. Terms capturing surgical mesh for inguinal hernia (e.g. “surgical mesh,” “polypropylene mesh”) were searched in combination with terms capturing the condition of interest (e.g. “groin hernia, “inguinal hernia”). The search was limited to exclude animal studies, conference abstracts, editorials, and letters. The full search strategy is reported in Appendix 1: Search Strategies for Systematic Review of Safety and Efficacy of Surgical Mesh for Inguinal Hernia Repair.

8.2.2 Study Selection

RCTs examining permanent and semi-permanent synthetic surgical mesh for inguinal hernia compared to biological mesh, suture repair, or dissolvable mesh were included. Abstracts were screened in duplicate by independent reviewers using *a priori* inclusion and exclusion criteria listed in Table 12. Abstracts that were included by either reviewer proceeded to full-text review. At the full-text review stage, studies were screened in duplicate by two reviewers, with any discrepancies resolved through discussion and consensus. Studies were excluded if they were not RCTs, were not purely for inguinal hernia, did not examine synthetic mesh compared to biological mesh, suture repair, or dissolvable mesh, were not available in English or French, did not report original data, or were animal studies. Studies were also excluded if they included female patients and did not stratify results by sex. Given the difference in incidence and anatomy between male and female inguinal hernia, studies that included some female patients but did not present results separately by sex were excluded.

8.2.3 Data Extraction

For all studies, year of publication, country, patient selection, patient characteristics, description of technologies, recurrence rates, and follow-up time were extracted using standardized data extraction forms. Safety outcomes consisting of complications (e.g., pain) were also extracted. Discrepancies between reviewers during data extraction were resolved through consensus.

8.2.4 Quality Assessment

During data extraction, each included study was assessed for quality using The Cochrane Risk of Bias Tool.[31] Quality assessment was completed in duplicate with discrepancies being resolved through discussion. Using this tool, each study was assessed across five potential domains of bias (randomization process, deviations from the intended interventions, missing outcome data, measurement of the outcome, and selection of the reported result). Each domain was assigned a "low, "high," or "some concern" risk of bias, based on the answers to the signaling questions.

8.2.5 Meta-Analysis

A meta-analysis was conducted for comparisons with two or more studies to inform the magnitude of treatment effect for synthetic surgical mesh for inguinal hernia with respect to recurrence rates and complications. The following comparator pairs were assessed: synthetic mesh vs. suture repair (e.g., Shouldice) and synthetic mesh vs. porcine tissue. For each study, the

number of participants who experienced recurrence and treatment complications were compared between the synthetic mesh and the comparator group stratified by follow-up time.

A random effects model using the method of DerSimonian and Laird [32] was used, with a continuity correction of 0.5 where appropriate. The same continuity correction was used to allow inclusion of zero-total event trials.[33] Separate analyses were conducted based on the comparator groupings established during data extraction (as outlined above). Meta-analyses were conducted using odds ratio to express the effectiveness of permanent synthetic surgical mesh in relation to other comparators. For studies only reporting a median follow-up time, normal distributions were assumed and median follow-up time value was used. Statistical analysis was completed in STATA 14.[34]

Table 12: Inclusion and Exclusion Criteria

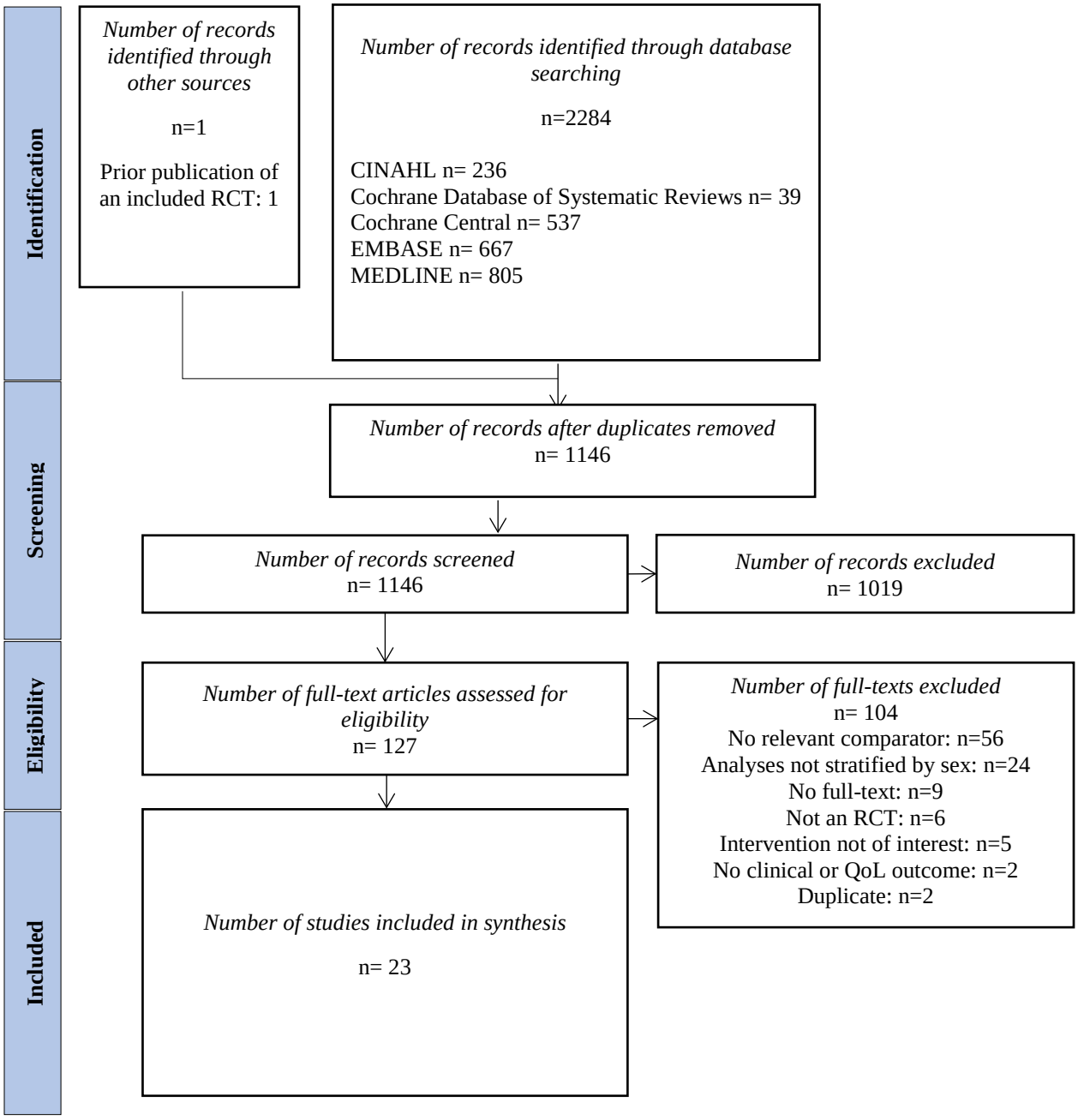
	Inclusion	**Exclusion**
Population	Adult population, male only or with results stratified by sex	Animal studies; pediatric population
Intervention	Assesses use of surgical mesh for inguinal hernia Assesses use of synthetic mesh • Polypropylene material • Permanent meshes • Semi-permanent meshes	• Assesses use of surgical mesh not for inguinal hernia • Does not assess surgical mesh • Assesses use of biological mesh, grafts • Assesses surgical technique for mesh fixation/implantation (e.g. laparoscopic vs open)
Comparator	Compares surgical mesh for hernia to: • Non-mesh surgical procedures • Conservative management • Other surgical meshes for hernia (porcine, tissue or dissolvable mesh)	• Surgical technique for mesh fixation/implantation (e.g. laparoscopic vs open)
Outcome	Clinical outcome- any; or QoL outcome	No clinical outcome; no QoL outcome
Design	RCT design- any	Not an RCT; RCT sub-analysis (without re-randomization)
	English or French	Not English or French
	Full-text available	No full-text

8.3 Results

A total of 2284 citations were identified from the literature search (see flowchart in Figure 4). Of those, 1146 were screened during abstract review, of which 1019 were excluded, and 127 proceeded to full-text review. A total of 104 articles were excluded at full-text review for the following reasons: 56 examined differences in surgical technique only, rather than differences in mesh; 24 did not stratify analyses by sex; nine were not available as full-text; six were not RCTs; five did not assess permanent synthetic mesh; two did not report clinical or QoL outcome; and two were duplicates. One study was identified during hand-searching of the included full-text publications (a prior study of one of the follow-up papers already included).

In total, 23 studies were included in the review (20 original RCTs and three follow-up studies). Three studies included three comparator arms, which have been grouped according to each intervention and specific comparator. Nineteen studies compared synthetic mesh to suture repair (e.g., Shouldice), and four studies compared synthetic mesh to porcine tissue.

Figure 4: PRISMA Flow-chart for Inguinal Hernia Review



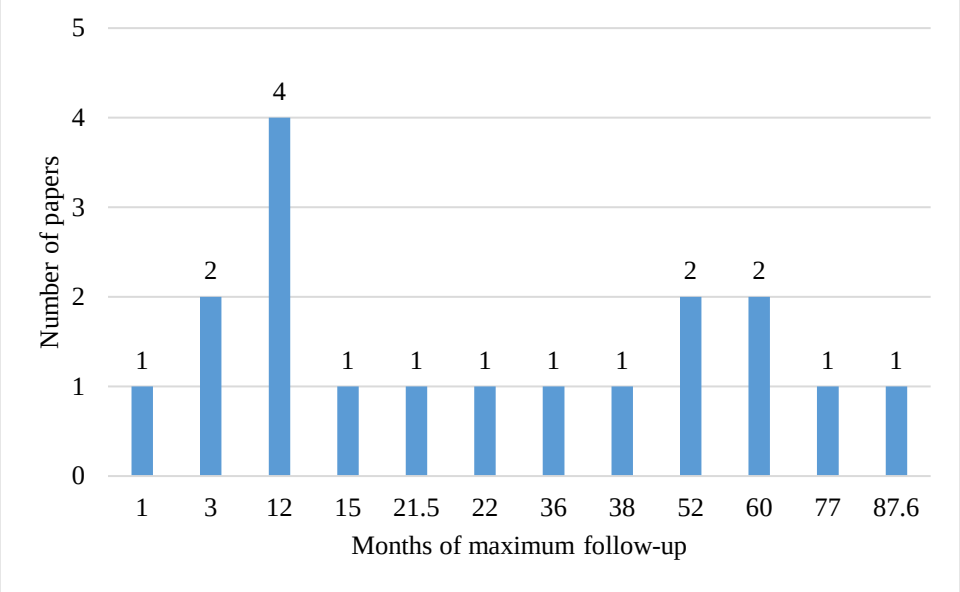
8.3.2 Synthetic Mesh vs Suture repair

8.3.2.1 Characteristics of Included Studies

Nineteen studies (16 original RCTs and three follow-up studies) examining synthetic mesh vs. suture repair were identified. Five studies were conducted in Sweden,[35-39] two in Egypt,[40,41] two in Germany,[42,43] and the rest of the studies were from Denmark,[44] India,[45] France,[46] Italy,[47] Australia,[48] Canada,[49] Pakistan,[50] USA,[51] Poland,[52] and Kenya.[53] The studies were published between 1998 and 2017, with the majority of the studies published in the late 1990s and early 2000s.

Maximum follow-up times across the synthetic mesh and suture repair studies included in the review ranged from 1 month to 87.6 months; 12 months was the most common follow-up time-point (see Figure 5). Lichtenstein was the most commonly used mesh surgery, and Shouldice was the most commonly used non-mesh surgery. Most study sample sizes ranged from 30-100 (~15 to ~50 patients per group), with one RCT and its follow-up studies examining close to 1000 participants across two treatment groups (~500 patients per group).[35-37] Common study inclusion criteria were male patients, ≥18 years old, with primary inguinal hernia. Recurrent hernia was a common exclusion criterion. Study characteristics are reported in Table A1 in Appendix 2: Characteristics of Included Studies.

Figure 5: Follow-up Times in Synthetic Mesh vs. Suture repair Studies, n=19



8.3.2.2 Quality of Included Studies

Of the 19 studies that compared mesh repair to suture repair, four were considered to be at high risk of bias from randomization, and another three were of some concern. In one of these studies,[44] bias from randomization was considered high because patient characteristics were used to assign patients to one of two studies drawing from the same pool of patients. In another study,[41] risk of bias was high because randomization was performed by odd or even patient registration numbers. In the other two papers, little information was provided about randomization techniques, and in both there were concerns over baseline imbalances in patient characteristics.[38,47]

Two studies were of moderate concern with respect to bias from deviation; in one, surgeons were of highly variable skill including some who were inexperienced at hernia repair.[51] In the other study, three Shouldice procedures were converted to Lichtenstein but the patients were analyzed in the Shouldice group.[39]

Three papers reported studies that were considered moderately concerning with regard to missing outcome data.[49,50,53] These papers presented little information about drop-out rates between the groups, or reasons for drop-outs.

Seven studies of the 19 assessed were considered to be at high risk for bias from measurement.[40,36,43,48,49,51,53] In each case, the primary outcome of the study was pain, which was assessed by patients who were not blinded to their allocation.

Lastly, one of the studies was considered to be at high risk of bias from reporting because it did not report complications arising at one year, despite assessing these complications.[38] Another study was also at high risk from reporting because patients were assessed by various methods, including by phone and examination by local physicians instead of study personnel.[51] Quality assessment for synthetic mesh vs. suture repair studies is reported in Table 13.

Table 13: Quality Assessment of Synthetic Mesh vs. Suture Repair

Study ID	Bias from Randomization	Bias from Deviation	Bias from Missing Outcome Data	Bias from Measurement	Bias in Reported Results
Abd El Maksoud, 2014[40]	**Low risk**	**Low risk**	**Low risk**	**High risk**	**Low risk**
Arvidsson, 2005[35]	**Low risk**	**Low risk**	**Low risk**	**Low risk**	**Low risk**
Berndsen, 2007[36]	**Low risk**	**Low risk**	**Low risk**	**High risk**	**Low risk**
Berndsen, 2002[37]	**Low risk**	**Low risk**	**Low risk**	**Low risk**	**Low risk**
Butters, 2007[42]	**Low risk**	**Low risk**	**Low risk**	**Low risk**	**Low risk**
Callesen, 1999[44]	**High risk**	**Low risk**	**Low risk**	**Low risk**	**Low risk**
Chakraborty, 2007[45]	**Some concern**	**Low risk**	**Low risk**	**Low risk**	**Low risk**
Damamme, 1998[46]	**Low risk**	**Low risk**	**Low risk**	**Low risk**	**Low risk**
Danielsson, 1999[38]	**High risk**	**Low risk**	**Low risk**	**Low risk**	**High risk**
Di Vita, 2000[47]	**High risk**	**Low risk**	**Low risk**	**Low risk**	**Low risk**
Elsebae, 2008[41]	**High risk**	**Low risk**	**Low risk**	**Low risk**	**Low risk**
Koninger, 2004[43]	**Low risk**	**Low risk**	**Low risk**	**High risk**	**Low risk**
Koukourou, 2001[48]	**Low risk**	**Low risk**	**Low risk**	**High risk**	**Low risk**

McGillicuddy, 1998[49]	**Low risk**	**Low risk**	**Some concern**	**High risk**	**Low risk**
Memon, 2017[50]	**Some concern**	**Low risk**	**Some concern**	**Low risk**	**Low risk**
Miedema, 2004[51]	**Low risk**	**Some concern**	**Low risk**	**High risk**	**High risk**
Nordin, 2002[39]	**Low risk**	**Some concern**	**Low risk**	**Low risk**	**Low risk**
Szopinski, 2012[52]	**Low risk**	**Low risk**	**Low risk**	**Low risk**	**Low risk**
Wamalwa, 2015[53]	**Some concern**	**Low risk**	**Some concern**	**High risk**	**Low risk**

8.3.2.3 Meta-analysis of Recurrence Rates

Two of the synthetic mesh vs. suture repair studies provided adequate data on recurrence rates to permit pooling at <1 year, seven provided data for pooling at 1-2 years, three provided data for pooling at 3-5 years, and three studies provided data for pooling at ≥18 months. Figure 6 shows the overall risk difference for recurrence rates (forest plot) in synthetic mesh vs. suture repair.

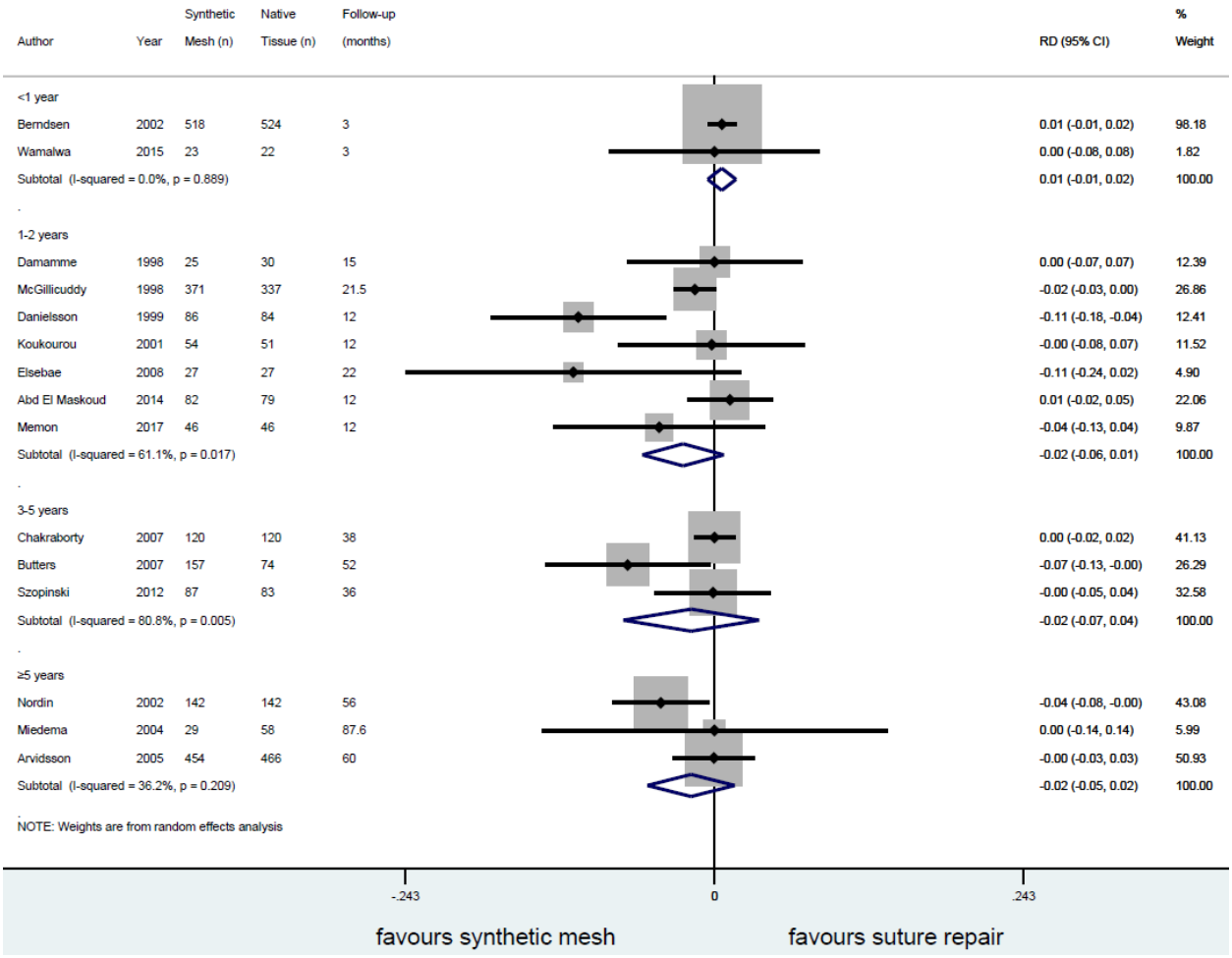
At <1 year, the overall risk difference is 0.01 (95% confidence interval [CI]: -0.01, 0.02), suggesting that the risk of experiencing recurrence at <1 year is 1% greater with synthetic mesh than with suture repair; however, this effect is not statistically significant because the CI of this pooled estimate crosses the null line (1.00).

The opposite is true for the overall risk differences of recurrence at 1-2 years, 3-5 years, and ≥5 years, which are -0.02 (95% CI: -0.06, 0.01), -0.02 (95% CI: -0.07, 0.04), and -0.02 (95% CI: -0.05, 0.02), respectively. These latter findings suggest that the risk of experiencing recurrence at 1-2 years, 3-5 years, and ≥5 years is 2% smaller with synthetic mesh than with suture repair; however, these effects are not significant and should be interpreted with caution because they are associated with moderate-to-substantial heterogeneity (i^2=61.1%, i^2=80.8%, and i^2=36.2%, respectively). It should be noted that, studies varied greatly in their sample size, ranging from 30-100 (~15 to ~50 patients per group), with one RCT and its follow-up studies examining close to

1000 participants across two treatment groups (~500 patients per group), which may have affected the heterogeneity in our analyses.

A funnel plot of publication bias was not generated due to the high heterogeneity across the studies, given that high heterogeneity can decrease the ability to detect publication bias.[54]

Figure 6: Forest Plot of Recurrence Rates in Patients with Inguinal Hernia Receiving Synthetic Mesh vs. Suture repair

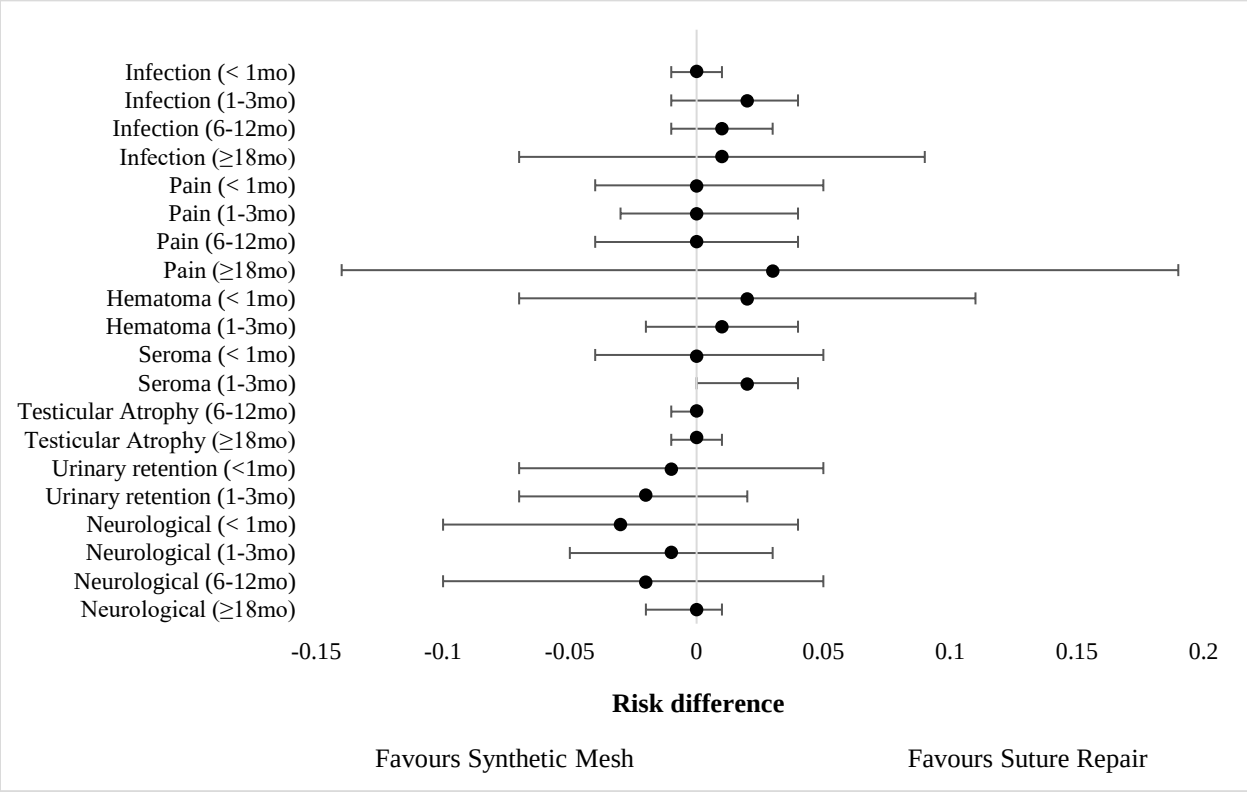


8.3.2.4 Meta-analysis of Complications

Sufficient data were available to conduct meta-analyses of seven complications reported in the synthetic mesh vs. suture repair studies: infection, hematoma, seroma, pain, testicular atrophy, urinary retention, and neurological complications (including neuralgia, neuritis, numbness, and nerve damage). Overall, the differences between synthetic mesh and suture repair groups with

respect to these complications were minor (0-3%) and not statistically significant. A summary of the risk differences is reported in Figure 7, with more granular details reported in the sections below; forest plots for the inguinal hernia complications analyses are reported in Appendix 3: Meta-Analysis Forest Plots.

Figure 7: Risk Differences for Complications in Inguinal Hernia Patients Receiving Synthetic Mesh vs. Suture repair



8.3.2.4.1 Infection

Infection was the most frequently reported intraoperative complication was reported in 10 studies.[37-41,45,48-50,52] Two of the synthetic mesh vs. suture repair studies provided adequate data on infection rates to permit pooling at <1 month,[37,48] four provided data for pooling at 1-3 months,[38-40,49] three provided data for pooling at 6-12 months,[40,50,52] and two studies provided data for pooling at ≥18 months[41,45] (see Figure A1 in Appendix 3).

At <1 month, the overall risk difference is 0.00, suggesting that there is no difference in rates of infection following synthetic mesh or suture repair surgeries. At 1-3 months, the overall risk difference is 0.02 (95% CI: -0.01, 0.04), suggesting that the risk of infection is 2% greater with synthetic mesh than with suture repair; however, this effect is not significant and is associated

with substantial heterogeneity (i^2=52.5%). At 6-12 months, the overall risk difference is 0.01 (95% CI: -0.01, 0.03), suggesting that the risk of infection is 1% greater with synthetic mesh than with suture repair; however, this effect is not significant. Lastly, at ≥18 months, the overall risk difference is 0.01 (95% CI: -0.07, 0.09), suggesting that the risk of infection is 1% greater with synthetic mesh than with suture repair; however, this effect is not significant and is associated with substantial heterogeneity (i^2=47.6%).

8.3.2.4.2 Pain

Pain was the most frequently reported intraoperative complication and was reported in nine studies.[37,39,43,44,49,51-53] Two of the studies provided adequate data on pain rates to permit pooling at <1 month,[37,53] four provided data for pooling at 1-3 months,[37,39,44,53] three provided data for pooling at 6-12 months,[39,49,52] and three provided data for pooling at ≥18 months[39,43,51] (see Figure A2 in Appendix 3). At <1 month and 1-3 months, the overall risk differences are 0.00, suggesting that there are no differences in rates of pain following synthetic mesh or suture repair surgeries. At 6-12 months, the overall risk difference is also 0.00, suggesting that there is no difference in rates of pain; however, this effect is associated with moderate heterogeneity (i^2=47.5%). Lastly, at ≥18 months, the overall risk difference is 0.03 (95% CI: -0.14, 0.19), suggesting that the risk of pain is 3% greater with synthetic mesh than with suture repair; however, this effect is not significant and is associated with substantial heterogeneity (i^2=83.5%).

8.3.2.4.3 Hematoma

Hematoma was reported in five of the synthetic mesh vs. suture repair studies.[39,46,48,50,51] Two of the studies provided adequate data on hematoma rates to permit pooling at <1 month[46,48] and two provided data for pooling at 1-3 months[39,51] (see Figure A3 in Appendix 3). Data for time-points that could not be pooled due to an insufficient number of studies are presented in the forest plot but were not meta-analyzed. At <1 month and 1-3 months, the overall risk differences are 0.02 (95% CI: -0.07, 0.11) and 0.01 (95% CI: -0.02, 0.04), respectively, suggesting that the risks of hematoma are 2% and 1% greater with synthetic mesh than with suture repair; however, these effects are not significant.

8.3.2.4.4 Seroma

Seroma was reported in five of the synthetic mesh vs. suture repair studies.[37,39,40,48,52] Two of the studies provided adequate data on seroma rates to permit pooling at <1 month[48,52] and four provided data for pooling at 1-3 months[37,39,40,52] (see Figure A4 in Appendix 3). At <1 month, the

overall risk difference is 0.00 suggesting that there is no difference in rates of seroma following synthetic mesh or suture repair surgeries. At 1-3 months, the overall risk difference is 0.02 (95% CI: -0.00, 0.04), suggesting that the risk of seroma is 2% greater with synthetic mesh than suture repair; however, this effect is not significant and is associated with substantial heterogeneity (i^2=62.7%).

8.3.2.4.5 Testicular Atrophy

Testicular atrophy was reported in four of the synthetic mesh vs. suture repair studies.[42,45,49,52] Two of the studies provided adequate data on testicular atrophy rates to permit pooling at 6-12 months[49,52] and two provided data for pooling at ≥18 months[42,45] (see Figure A5 in Appendix 3). The overall risk differences for both those time-points are 0.00, suggesting that there are no differences in rates of testicular atrophy following synthetic mesh or suture repair surgeries.

8.3.2.4.6 Urinary Retention

Urinary retention was reported in five of the synthetic mesh vs. suture repair studies.[38,40,46,48,53] Three of the studies provided adequate data on urinary retention rates to permit pooling at <1 month[46,48,53] and two provided data for pooling at 1-3 months[38,40] (see Figure A6 in Appendix 3). At <1 month and 1-3 months, the overall risk differences are -0.01 (95% CI: -0.07, 0.05) and -0.02 (95% CI: -0.07, 0.02), respectively, suggesting that the risks of urinary retention are 1% and 2% smaller with synthetic mesh than with suture repair; however, these effects are not significant.

8.3.2.4.7 Neurological Complications

The category of neurological complications included neuralgia, neuritis, numbness, loss of sensation, and nerve compression/damage, which were reported in seven studies.[37,42,45,46,48,49,52] Two of the studies provided adequate data to permit pooling at <1 month,[46,48] two provided data for pooling at 1-3 months,[37,49] three provided data for pooling at 6-12 months, [48,49,52] and three provided data for pooling at ≥18 months[42,45,52] (see Figure A7 in Appendix 3).

At <1 month, the overall risk difference is -0.03 (95% CI: -0.10, 0.04), suggesting that the risk of neurological complications is 3% smaller with synthetic mesh than with suture repair; however, this effect is not significant.

At 1-3 months, the overall risk difference is -0.01 (95% CI: -0.05, 0.03), suggesting that the risk of neurological complications is 1% smaller with synthetic mesh than with suture repair;

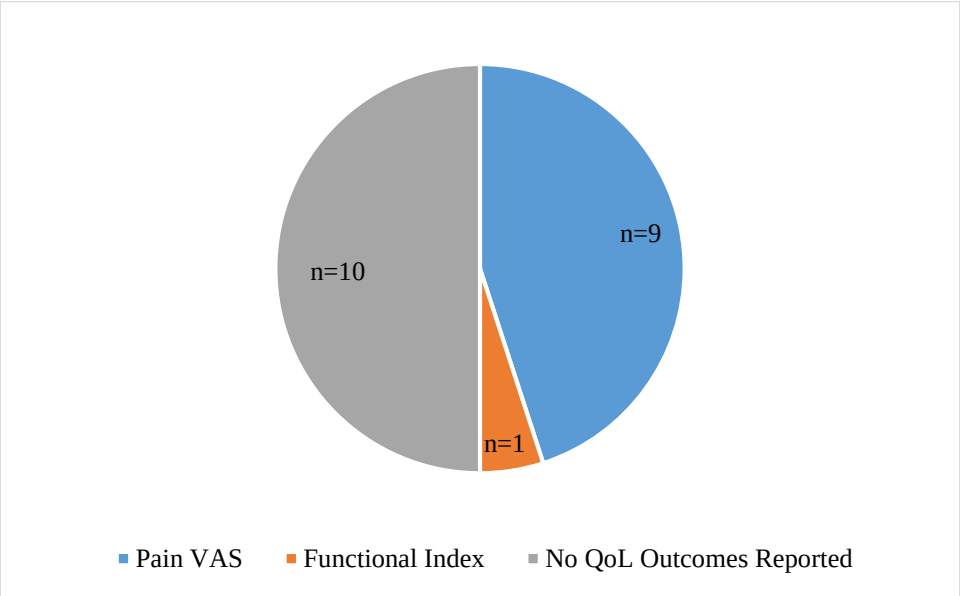
however, this effect is not significant and is associated with considerable heterogeneity (i^2=89.6%).

At 6-12 months, the overall risk difference is -0.02 (95% CI: -0.10, 0.05), suggesting that the risk of neurological complications is 2% smaller with synthetic mesh than with suture repair; however, this finding is not significant and is associated with moderate heterogeneity (i^2=41.3%). Lastly, at ≥18 months, the overall risk difference is 0.00, suggesting that there are no differences in rates of neurological complications following synthetic mesh or suture repair surgeries.

8.3.2.5 Subjective Outcomes

Only nine of the studies examining synthetic mesh vs. suture repair reported validated patient-reported measures. These measures consisted of pain VAS scores and the Functional Index (one study); see Figure 8. In general, patients in the synthetic mesh group reported less pain on the VAS than in the suture repair group. However, in two studies, the opposite trend was observed, wherein synthetic mesh patients reported significantly[40] and not-significantly[48] more pain than the suture repair group. Many studies assessed the number of days taken to return to work after surgery; however, because it was not assessed using a validated clinical measure, this outcome was not examined in our review.

Figure 8: Patient-reported Outcome Measures across the Synthetic Mesh vs. Suture Repair Studies, n=19



*"n" indicates number of studies that reported the subjective outcome measure (some studies reported more than one)

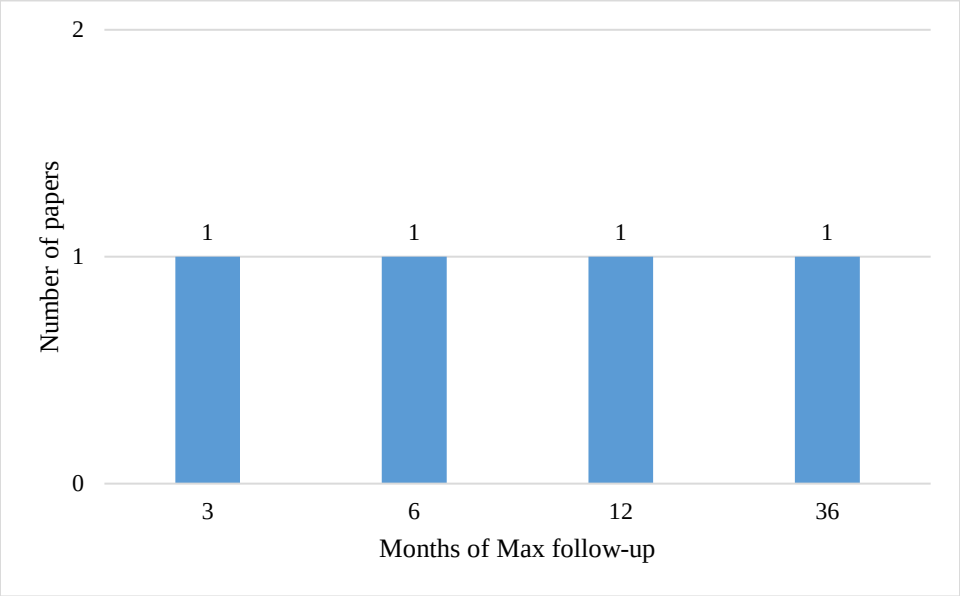
8.3.3 Synthetic Mesh vs Porcine

8.3.3.1 Characteristics of Included Studies

Four studies (all original RCTs) examining synthetic mesh vs. porcine were identified. Three studies examined permanent synthetic mesh, and one study examined semi-permanent mesh.[55] Two studies were conducted in Italy in 2003[56] and 2009,[57] and two studies were conducted in the US in 2013[58] and 2014.[55] Maximum follow-up times ranged from 3 to 36 months (see Figure 9).

Study sample sizes ranged from 20 (~10 patients per group) to 170 (~85 patients per group). Common study inclusion criteria were male patients, ≥18 years old, with primary inguinal hernia. Common exclusion criteria were recurrent hernia, hypersensitivity to drugs used in the study, and any condition preventing the evaluation of pain. Study characteristics are reported in Table A2 in Appendix 2: Characteristics of Included Studies.

Figure 9: Follow-up Times in Synthetic Mesh vs. Porcine Mesh Studies, n=4



8.3.3.2 Quality of Included Studies

Of the four studies assessing synthetic vs. porcine mesh, one was considered to be at high risk of bias from randomization because randomization was accomplished by a "voice recognition system," and significantly more patients in one group were diagnosed with diabetes.[55] Another study was considered to be of some concern due to missing information on randomization.[56] That same study was also of some concern for bias due to missing outcome data due to providing little information about drop-out rates, proportions of drop-outs between the groups, or reasons for drop-outs, as well as high risk for bias due to unclear reporting of follow-up times and paucity of outcome data.[56] All of the studies examining synthetic vs. porcine mesh were considered to be at low risk of bias from deviation and bias from measurement. Quality assessment for synthetic mesh vs. porcine mesh studies is reported in Table 14.

Table 14: Quality Assessment of Synthetic Mesh vs. Porcine Mesh

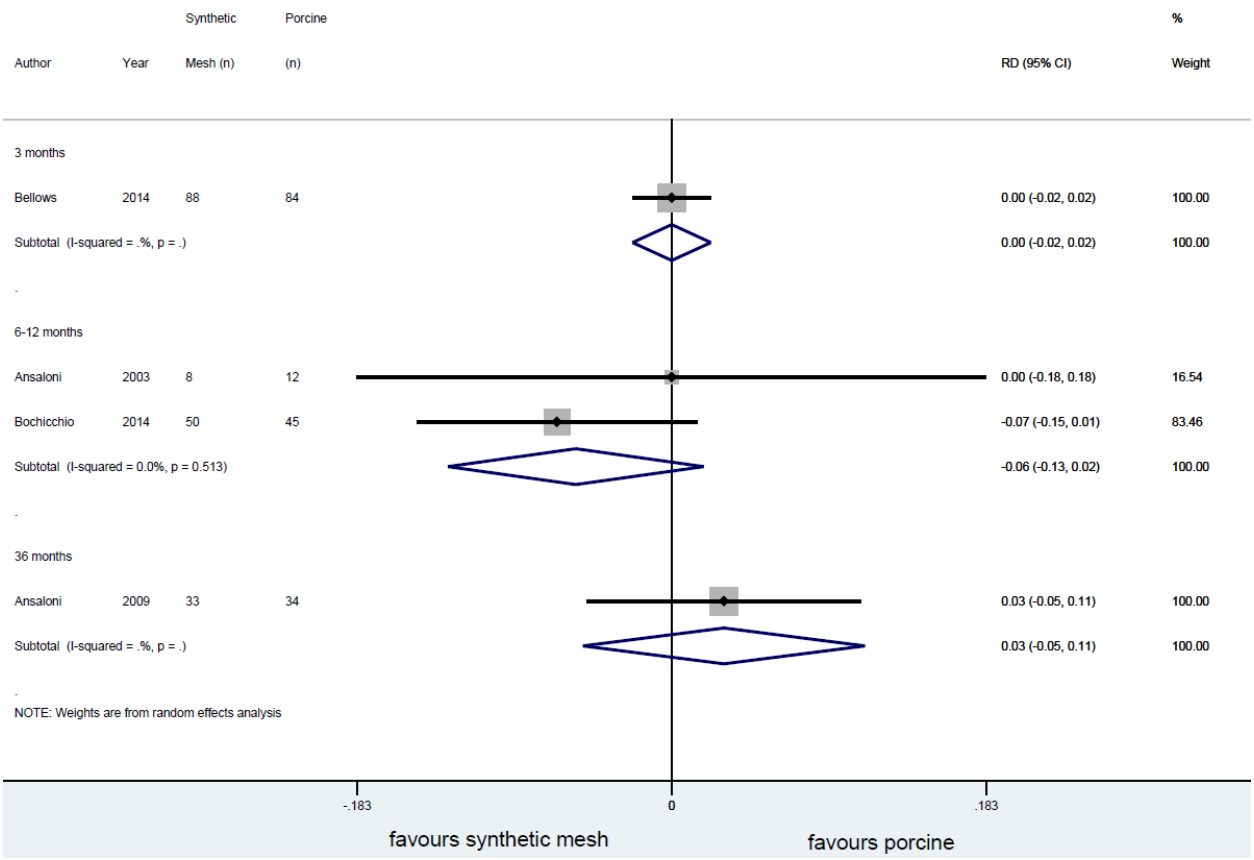
Study ID	Bias from Randomization	Bias from Deviation	Bias from Missing Outcome Data	Bias from Measurement	Bias in Reported Results
Ansaloni, 2009[57]	**Low risk**	**Low risk**	**Low risk**	**Low risk**	**Low risk**
Ansaloni, 2003[56]	**Some concern**	**Low risk**	**Some concern**	**Low risk**	**High risk**

Bellows, 2014[58]	**Low risk**	**Low risk**	**Low risk**	**Low risk**	**Low risk**
Bochicchio, 2014[55]	**High risk**	**Low risk**	**Low risk**	**Low risk**	**Low risk**

8.3.3.3 Meta-analysis of Recurrence Rates

Two of the synthetic mesh vs. porcine studies provided adequate data on recurrence rates to permit pooling at 6-12 months. Figure 10 shows the overall risk difference for recurrence rates (forest plot) in synthetic mesh vs. porcine mesh. Data for the time-points that could not be pooled due to an insufficient number of studies are presented in the forest plot but were not meta-analyzed. At 6-12 months, the overall risk difference is -0.06 (95% CI: -0.13, 0.02), suggesting that the risk of recurrence is 6% smaller with synthetic mesh than with porcine mesh; however, this finding is not significant because the CI of this pooled estimate crosses the null line (1.00). A funnel plot of publication bias was not generated due to an insufficient number of studies.

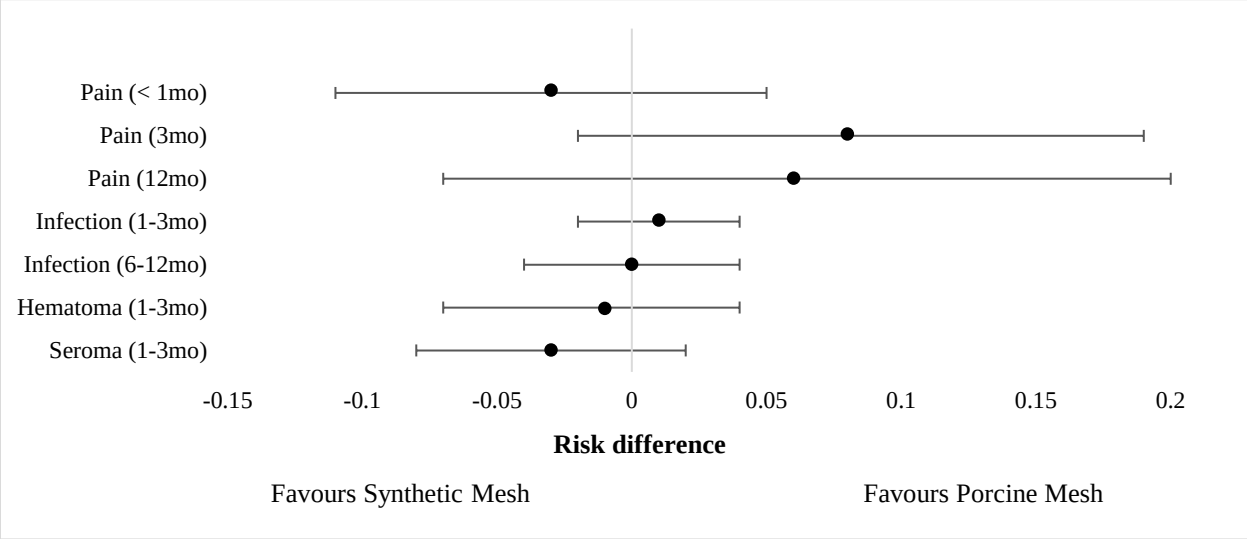
Figure 10: Forest Plot of Recurrence Rates in Patients with Inguinal Hernia Receiving Synthetic Mesh vs. Porcine Mesh



8.3.3.4 Meta-analysis of Complications

Sufficient data were available to conduct meta-analyses of four complications reported in the synthetic mesh vs. porcine mesh studies: pain, infection, hematoma, and seroma. Overall, the differences between synthetic mesh and porcine mesh groups with respect to these complications were minor (0-8%) and not statistically significant. The risk of pain at <1 month was 3% smaller with synthetic mesh than with porcine mesh, but the risk of pain at 3 and 12 months was 6% and 8% greater with synthetic mesh; however, these effects are not significant. A summary of the risk differences is reported in Figure 11, with more granular details reported in the sections below; forest plots for the inguinal hernia complications analyses are reported in Appendix 3: Meta-Analysis Forest Plots.

Figure 11: Risk Differences for Complications in Inguinal Hernia Patients Receiving Synthetic Mesh vs. Porcine Mesh



8.3.3.4.1 Infection

Infection was reported in three studies.[55,56,58] Two studies provided adequate data on infection rates to permit pooling at 1-3 months,[56,58] and two studies provided data for pooling at 6-12 months[55,56] (see Figure A8 in Appendix 3). Data for one time-point that could not be pooled (1 week) due to an insufficient number of studies are presented in the forest plot but were not meta-analyzed. At 1-3 months, the overall risk difference is 0.01 (95% CI: -0.02, 0.04), suggesting that 1% fewer patients experience infection in the porcine mesh group than in the synthetic mesh group. At 6-12 months, the overall risk difference is 0.00, suggesting that there is no difference in rates of infection following synthetic mesh or porcine mesh surgeries.

8.3.3.4.2 Pain

Pain was reported in three studies.[55,57,58] Two of the studies provided adequate data on pain rates to permit pooling at <1 month,[55,57] two provided data for pooling at 3 months,[57,58] and two provided data for pooling at 12 months[55,57] (see Figure A9 in Appendix 3). Data for time-points that could not be pooled due to an insufficient number of studies are presented in the forest plot but were not meta-analyzed. At <1 month, the risk difference is -0.03 (95% CI: -0.11, 0.05), suggesting that the risk of pain is 3% smaller with synthetic mesh than with porcine mesh; however, this effect is not significant. At 3 months, the risk difference is 0.08 (95% CI: -0.02, 0.19), suggesting that the risk of pain is 8% greater with synthetic mesh than with porcine mesh; however, this effect is not significant. Lastly, at 12 months, the risk difference is 0.06 (95% CI: -

0.07, 0.19), suggesting that the risk of pain is 6% greater with synthetic mesh than with porcine mesh; however, this effect is not significant and is associated with moderate heterogeneity (i^2=53.5%).

8.3.3.4.3 Hematoma

Hematoma was reported in three studies.[55,57,58] Two of the studies provided adequate data on hematoma rates to permit pooling at 1-3 months[57,58] (see Figure A10 in Appendix 3). Data for time-points that could not be pooled due to an insufficient number of studies are presented in the forest plot but were not meta-analyzed. The risk difference at 1-3 months is -0.01 (95% CI: -0.07, 0.04), suggesting that the risk of hematoma is 1% smaller with synthetic mesh than with porcine mesh; however, this effect is not significant.

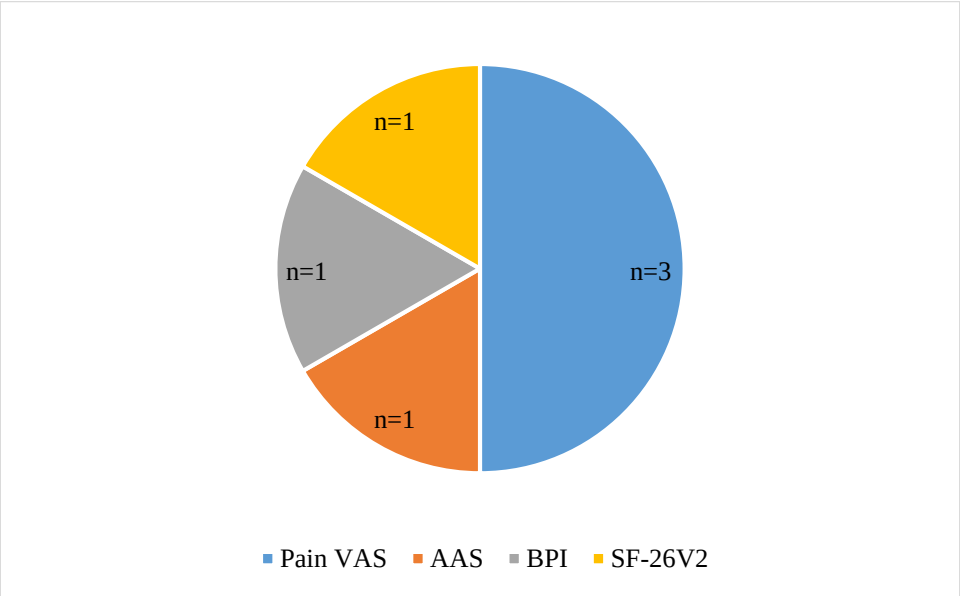
8.3.3.4.4 Seroma

Seroma was reported in three studies.[55,57,58] Two of the studies provided adequate data on seroma rates to permit pooling at 1-3 months[57,58] (see Figure A11 in Appendix 3). Data for time-points that could not be pooled due to an insufficient number of studies are presented in the forest plot but were not meta-analyzed. The risk difference at 1-3 months is -0.03 (95% CI: -0.08, 0.02), suggesting that the risk of seroma is 3% smaller with synthetic mesh than with porcine mesh; however, this effect is not significant.

8.3.3.5 Subjective Outcomes

All of the four studies examining synthetic mesh vs. porcine mesh reported patient-reported measures. These measures consisted of pain VAS scores, Brief Pain Inventory (BPI), Activities Assessment Scale (AAS), and the 36-Item Short Form Health Survey (SF-36) Version 2 (see Figure 12). In general, patients in the synthetic mesh group reported less post-operative pain on the VAS and impairment than in the porcine mesh group, with the exception of one study that found that synthetic mesh was associated with more pain at post-op than porcine mesh.[56] Many studies assessed the number of days taken to return to work after surgery; however, because it was not assessed using a validated clinical measure, this outcome was not examined in our review.

Figure 12: Patient-reported Outcome Measures across the Synthetic Mesh vs. Porcine Mesh Studies, n=4



*"n" indicates number of studies that reported the subjective outcome measure (some studies reported more than one)

8.4 Conclusion

Twenty-three (20 original RCTs and three follow-up studies) were identified that evaluated the effectiveness of synthetic surgical mesh against a comparator of interest. Of these studies, 19 studies compared synthetic mesh to suture repair and four compared synthetic mesh to porcine mesh.

At <1 year, the overall risk difference is 0.01 (95% confidence interval [CI]: -0.01, 0.02), suggesting that the risk of experiencing recurrence at <1 year is 1% greater with synthetic mesh than with suture repair; however, this effect is not statistically significant because the CI of this pooled estimate crosses the null line (1.00).

A meta-analysis of recurrence rates using risk differences found that the risk of recurrence at <1 year is 1% greater with synthetic mesh than with suture repair but is 2% smaller at 1-2 years, 3-5 years, and ≥5 years. These effects are not significant and the three latter should be interpreted with caution, as they are associated with moderate-to-substantial heterogeneity. It should be noted that the synthetic mesh vs. suture repair studies varied greatly in their sample size, ranging from 30-100 (~15 to ~50 patients per group), with one RCT and its follow-up studies examining

close to 1000 participants across two treatment groups (~500 patients per group), which may have affected the heterogeneity in our analyses. A meta-analysis of recurrence rates at 6-12 months using risk differences found that the risk of recurrence is 6% smaller with synthetic mesh than with porcine mesh; however, this effect is not significant.

Meta-analyses of complications for synthetic mesh vs. suture repair were conducted for infection, pain, hematoma, seroma, testicular atrophy, urinary retention, and neurological complications. Overall, the differences between synthetic mesh and suture repair groups with respect to these complications were minor (0-3%) and not statistically significant. Meta-analyses of complications for synthetic vs. porcine mesh were conducted for infection, pain, hematoma, and seroma. Similar to suture repair, the differences between synthetic mesh and porcine mesh groups with respect to these complications were minor (0-8%) and not statistically significant. The risk of pain was 3% smaller with synthetic mesh than with porcine mesh at <1 month, but 6% and 8% greater with synthetic mesh than with porcine mesh at 3 and 12 months, respectively; these effects are not significant.

Many of the included studies were of good quality, as assessed by the Cochrane Risk of Bias tool;[31] however, several studies were considered to be of high risk of bias either due to randomization, bias from measurement, or reporting of results, and some studies were of some concern for bias to do deviation and missing outcome data. Notably, several studies were considered to be at high risk of bias from measurement because their primary outcome (pain) was assessed by patients who were not blinded to their treatment group.

The outcomes most commonly reported within the included RCTs were recurrence and complications (primarily pain), which are considered to be clinically relevant outcomes. Very few studies reported validated QoL outcomes beyond pain VAS scores, which made it difficult to draw conclusions regarding the impact of synthetic mesh on patient-reported QoL across comparison groups.

The majority of the studies were conducted in Sweden, and only one study comparing synthetic mesh to suture repair was conducted in Canada. However, there is no reason to suspect that the patient mix and underlying etiology of inguinal hernia are substantially different in Canada. As such, the findings from this review should be generalizable to the Canadian context.

9 Conclusion

Safety and effectiveness of synthetic surgical mesh has been an emerging issue in the context of urogynecological repair. As such, the current HTA was conducted to distill the existing body of grey and peer-reviewed literature to examine the use of synthetic surgical mesh for inguinal hernia repair.

The environmental scan found that many inguinal hernia meshes are available for implantation in Canada and the United States. Unlike surgical meshes for stress urinary incontinence and pelvic organ prolapse repair, no broad actions against the use of mesh for inguinal hernia repair have been taken by the countries included in this analysis; however, certain products have been banned in Canada and the United States. A system for monitoring long-term complications associated with surgical mesh repair is crucial for establishing the risks associated with these devices. A new Action Plan on medical devices, which was published by Health Canada in 2018 will aim to intensify the pre-market approval process, increase post-market surveillance, and enhance the transparency of approval and surveillance of medical devices, including surgical synthetic mesh for inguinal hernia repair.

The guideline review identified two guidelines for treatment of inguinal hernia. The most recent guideline was published by the HerniaSurge Group in 2018 and has been endorsed by hernia organizations such as the EHS and the IEHS. Given that surgical mesh is the standard treatment for inguinal hernia, guideline recommendations focused largely on choice of technique for different populations and hernia types, as well as choice of mesh materials. Surgical mesh, particularly using a laparoscopic/laparo-endoscopic technique, was recommended by both guidelines. Consistent with the guideline recommendations, one of the HTAs identified as part of this review (n=2) found that laparoscopic repair was more clinically effective than open mesh repair; the other HTA found that open preperitoneal mesh repair was more clinically effective than Lichtenstein mesh repair.

The systematic review of the peer-reviewed literature identified 20 unique RCTs and three follow-up studies evaluating the effectiveness of synthetic surgical mesh vs. suture repair (n=19) and porcine mesh (n=4). Studies ranged from 1 to 87.6 months of maximum follow-up time, and 12 months was the most common follow-up time-point.

Analyses of the inguinal hernia literature suggest that, with respect to risk of recurrence, synthetic mesh is not significantly better than porcine mesh at 6-12 months (RD=-0.06 [95% CI: -0.13, 0.02]). Synthetic mesh is also not significantly better than suture repair with respect to risk of recurrence at <1 year (RD=0.01 [95% CI: -0.01, 0.02]), 1-2 years (RD=-0.02 [95% CI: -0.06, 0.01]), 3-5 years (RD=-0.02 [95% CI: -0.07, 0.04]) and ≥5 years (RD=-0.02 [95% CI: -0.05, 0.02]); however, the effects for the three latter time-points for the suture repair comparison should be interpreted with caution due to heterogeneity in the meta-analysis.

Commonly reported complications for the synthetic mesh vs. suture repair comparison were infection, pain, hematoma, seroma, testicular atrophy, urinary retention, and neurological complications, which were not significantly different across the two groups (all 0-3% differences). For the synthetic vs. porcine mesh comparison, infection, pain, hematoma, and seroma were the most commonly reported complications and did not significantly differ across the two groups (all 0-8% differences); the risk of pain was 3% smaller with synthetic mesh than with porcine mesh at <1 month, but 6% and 8% greater with synthetic mesh than with porcine mesh at 3 and 12 months, respectively; these effects are not significant.

While relatively robust meta-analysis comparisons could be made for the synthetic mesh vs. suture repair groups at the 1-2 years follow-up point, there were generally few studies (~2-3) for the remainder of the time-points for the suture repair comparison, as well as the comparison with porcine mesh. Furthermore, evidence on patient-reported QoL using validated measures was scarce. Overall, analyses of recurrence rates suggest that synthetic mesh is similar to suture repair (however, these results are associated with moderate-to-substantial heterogeneity after 1 year) and is comparable to porcine mesh. Risk profile of complications is similar and not significant across synthetic mesh and its comparators.

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11 Appendices

Appendix 1: Search Strategies for Systematic Review of Safety and Efficacy of Surgical Mesh for Inguinal Hernia Repair

MEDLINE- 805 abstracts

1. Hernia, Inguinal/
2. (inguinal* adj5 hernia*).tw,kf.
3. (groin adj5 hernia*).tw,kf.
4. 1 or 2 or 3
5. Surgical Mesh/
6. Suburethral Slings/
7. (fascial sling* or mesh or mesh plug* or mesh kit* or mesh sling* or mid-urethral sling* or midurethral sling* or mini-sling* or polypropylene mesh* or Prolene or pubovaginal sling* or retropubic sling* or sling surger* or suburethral sling* or suburethral tape* or surgical mesh* or synthetic mesh* or tension-free sling*or tension-free vaginal tape* or transobturator sling* or trans-obturator sling* or transobturator tape* or trans-obturator tape* or transvaginal mesh*or Ultrapro or urethral sling* or vaginal tape* or Vypro).tw,kf.
8. 5 or 6 or 7
9. 4 and 8
10. limit 9 to (english or french)
11. animals/ not humans/
12. 10 not 11
13. limit 12 to (editorial or letter)
14. 12 not 13
15. randomized controlled trial.pt.
16. controlled clinical trial.pt.
17. (groups or placebo* or random* or trial or trials).tw,kf.
18. 15 or 16 or 17
19. 14 and 18

EMBASE- 667 abstracts

1. inguinal hernia/
2. (inguinal* adj5 hernia*).tw,kw.
3. (groin adj5 hernia*).tw,kw.
4. 1 or 2 or 3
5. exp surgical mesh/
6. (fascial sling* or mesh or mesh plug* or mesh kit* or mesh sling* or mid-urethral sling* or midurethral sling* or mini-sling* or polypropylene mesh* or Prolene or pubovaginal sling* or retropubic sling* or sling surger* or suburethral sling* or suburethral tape* or surgical mesh* or

synthetic mesh* or tension-free sling*or tension-free vaginal tape* or transobturator sling* or trans-obturator sling* or transobturator tape* or trans-obturator tape* or transvaginal mesh*or Ultrapro or urethral sling* or vaginal tape* or Vypro).tw,kw.
7. 5 or 6
8. 4 and 7
9. limit 8 to (english or french)
10. limit 9 to animal studies
11. limit 9 to (human and animal studies)
12. 10 not 11
13. 9 not 12
14. limit 13 to (randomized controlled trial or controlled clinical trial)
15. crossover-procedure/ or double-blind procedure/ or randomized controlled trial/ or single-blind procedure/
16. (random* or factorial* or crossover* or cross over* or placebo* or (doubl* adj blind*) or (singl* adj blind*) or assign* or allocate* or volunteer*).tw,kw.
17. 15 or 16
18. 13 and 17
19. 14 or 18
20. limit 19 to conference abstract
21. 19 not 20

CINAHL- 236 abstracts

1. (MH "Hernia, Inguinal") OR TI (inguinal* N5 hernia*) OR AB (inguinal* N5 hernia*) OR TI (groin N5 hernia*) OR AB (groin N5 hernia*)
2. ((MH "Surgical Mesh") OR (MH "Suburethral Slings")) OR TI ((fascial sling* or mesh plug* or mesh kit* or mesh sling* or mid-urethral sling* or mini-sling* or polypropylene mesh* or Prolene or pubovaginal sling* or retropubic sling* or sling surger* or suburethral sling* or suburethral tape* or surgical mesh*or synthetic mesh* or tension-free sling*or tension-free vaginal tape* or transobturator sling* or trans-obturator sling* or transobturator tape* or trans-obturator tape* or transvaginal mesh*or Ultrapro or urethral sling* or vaginal tape* or Vypro)) OR AB ((fascial sling* or mesh plug* or mesh kit* or mesh sling* or mid-urethral sling* or mini-sling* or polypropylene mesh* or Prolene or pubovaginal sling* or retropubic sling* or sling surger* or suburethral sling* or suburethral tape* or surgical mesh*or synthetic mesh* or tension-free sling*or tension-free vaginal tape* or transobturator sling* or trans-obturator sling* or transobturator tape* or trans-obturator tape* or transvaginal mesh*or Ultrapro or urethral sling* or vaginal tape* or Vypro))
3. 1 and 2
4. Limit 3 to (English or French) and scholarly peer-reviewed articles
5. Limit 4 to randomized controlled trial

6. TI ((groups or placebo* or random* or trial or trials)) OR AB ((groups or placebo* or random* or trial or trials))
7. 4 and 6
8. 5 or 7

Cochrane CENTRAL- 537 abstracts

1. Hernia, Inguinal/
2. (inguinal* adj5 hernia*).tw,kf.
3. (groin adj5 hernia*).tw,kf.
4. 1 or 2 or 3
5. Surgical Mesh/
6. Suburethral Slings/
7. (fascial sling* or mesh or mesh plug* or mesh kit* or mesh sling* or mid-urethral sling* or midurethral sling* or mini-sling* or polypropylene mesh* or Prolene or pubovaginal sling* or retropubic sling* or sling surger* or suburethral sling* or suburethral tape* or surgical mesh* or synthetic mesh* or tension-free sling*or tension-free vaginal tape* or transobturator sling* or trans-obturator sling* or transobturator tape* or trans-obturator tape* or transvaginal mesh*or Ultrapro or urethral sling* or vaginal tape* or Vypro).tw,kf.
8. 5 or 6 or 7
9. 4 and 8
10. limit 9 to (english or french)

Cochrane database- 39 abstracts

1. (inguinal* adj5 hernia*).tw,kf.
2. (groin adj5 hernia*).tw,kf.
3. (fascial sling* or mesh or mesh plug* or mesh kit* or mesh sling* or mid-urethral sling* or midurethral sling* or mini-sling* or polypropylene mesh* or Prolene or pubovaginal sling* or retropubic sling* or sling surger* or suburethral sling* or suburethral tape* or surgical mesh* or synthetic mesh* or tension-free sling*or tension-free vaginal tape* or transobturator sling* or trans-obturator sling* or transobturator tape* or trans-obturator tape* or transvaginal mesh*or Ultrapro or urethral sling* or vaginal tape* or Vypro).tw,kf.
4. 1 or 2
5. 3 and 4

Appendix 2: Characteristics of Included Studies

Table A1: Characteristics of Synthetic Mesh vs. Suture Repair Studies Included in the Inguinal Hernia Review

Author, Country, Year	Inclusion criteria	Exclusion criteria	Control vs intervention	Follow-up times	Control patient characteristics	Intervention patient characteristics
Abd El Maksoud Egypt 2014[40]	male, 18-60 years old, primary inguinal hernia, Gilbert III or IV	NR	Modified darn repair vs Lichtenstein	3, 6 months, 1 year	n= 108 %male: 100 age: 37.47 11.97	n= 119 %male: 100 age: 37.44 11.93
Arvidsson, Sweden, 2005 (See Berndsen 2002[37], 2007[36])[35]	Men aged 30-70 years, primary unilateral inguinal hernia	ASA grade IV and V, scrotal hernia, previous major abdominal surgery, language difficulties and mental disturbance.	Shouldice vs TAPP with Prolene	7 days, 3 months, 1, 2, 3, 5 years	n= 466 %male: 100 age: 52.2 ± 10.7	n= 454 %male: 100 age: 54.2 ± 10.5
Berndsen, Sweden, 2007 (See Berndsen 2002[37], Arvidsson 2005[35])[36]	Male patients between 30 and 70 years with unilateral primary inguinal hernia	History of multiple abdominal operations or concomitant disease contraindicating general anesthesia	Shouldice vs TAPP with Prolene	7 days, 3 months, 1, 2, 3, 5 years (this paper presents 5 years	n= 431 %male: 100 age: 52 ± 10.7	n= 436 %male: 100 age: 51 ± 10.5
Berndsen, Sweden, 2002 (see Arvidsson 2005,[35] Berndsen 2007[36])[37]	Male patients between 30 and 70 years with unilateral primary inguinal hernia	Contraindications to laparoscopic surgery, such as multiple previous abdominal operations, bleeding diathesis, contraindications for general anesthesia, unable to participate in postoperative follow up because	Shouldice vs TAPP with Prolene	1, 2, 3, 5 7 days, regularly for 12 weeks	n=524 %male: 100 age: 52±10.6	n=518 %male: 100 age: 51±10.6

		of drug abuse, psychiatric disorders or language difficulties				
Butters, Germany, 2007 (See Koninger 2004[43])[42]	Male patients with primary inguinal hernia	NR	Shouldice vs. Lichtenstein with heavyweight polypropylene mesh	Median= 52 months (46-60)	n= 93 %male: 100 age: 56 (25–75)	n= 93 %male: 100 age: 53 (26–74)
Butters, Germany, 2008 (See Koninger 2004[43])[42]	Male patients with primary inguinal hernia	NR	Shouldice vs. TAPP with heavyweight polypropylene	Median= 52 months (46-60)	n= 93 %male: 100 age: 56 (25–75)	n= 94 %male: 100 age: 53 (30–74)
Callesen, Denmark, 1999[44]	Men referred for elective repair of a reducible indirect inguinal hernia, aged 18 to 75 years, inguinal ring >1.5cm	NR	Extirpation plus annulorrhaphy vs modified Lichtenstein	1, 4 weeks	n= 32 %male: 100 age: 49 (38–60)	n= 29 %male: 100 age: 51 (37–68)
Chakraborty, India, 2007[45]	Unilateral inguinal hernias, which were nonobstructive, reducible and either primary or recurrent	Bilateral inguinal hernias or presented with complications of inguinal hernia (obstruction, strangulation)	Abrahamson's technique (Darn) vs. Lichtenstein with polypropylene mesh	1,3,6,9, 12,18 months	n= 120 %male: 100 age: 40 (18-76)	n= 120 %male: 100 age: 38 (18-70)
Damamme, France, 1998[46]	Male patients older than 35 years, unilateral or bilateral, non-recurring, uncomplicated inguinal hernia, prior abdominal surgery, contraindications to	NR	Shouldice vs laparoscopy with polypropylene mesh	16 months	n= 30 %male: 100 age: 57 (38-76)	n= 25 %male: 100 age: 55.4 (36-74)

	laparoscopy, refused randomization					
Danielsson, Sweden, 1999[38]	Male patients with inguinal hernia	Incarcerated inguinal hernia or in need of emergency operation	Shouldice vs Lichtenstein with polypropylene mesh (Meadox)	3 weeks, 1, 3, 5 year	n= 89 %male: 100 age: 56 ± 16	n= 89 %male: 100 age: 58 ± 14
Di Vita, Italy, 2000[47]	Male patients, age range 25 to 60 years, unilateral inguinal hernia	Patients with metabolic, endocrine, hepatic or renal disease	Bassini vs Lichtenstein with Prolene	6, 24, 48, and 168 hours	n= 14 %male: 100 age: 55 ± 12	n= 16 %male: 100 age: 50 ± 18
Elsebae, Egypt, 2008[41]	18 years or older, submitted to emergency because of strangulated inguinal hernia	Recurrent hernia, preoperative peritonitis, inflamontary hernia and/or associated other hernias or intraabdominal masses or ascites	Bassini technique vs. Lichtenstein with polypropylene mesh	mean = 22 ± 6 months	n= 27 %male: 100 age: 43.2 (36–68)	n= 27 %male: 100 age: 34.6 (21–63)
Koninger, Germany, 2014 (See Butters 2008[42])[43]	Male patients with primary inguinal hernia	NR	Shouldice vs Lichtenstein with heavyweight polypropylene mesh	median of 52 months	n= 93 %male:100 age: 53 (25-75)	n= 93 %male:100 age: 53 (26-74)
Koninger, Germany, 2014 (See Butters 2008[42])[43]	Male patients with primary inguinal hernia	NR	Shouldice vs TAPP with heavyweight polypropylene mesh	median of 52 months	n= 93 %male:100 age: 53 (25-75)	n= 94 %male: 100 age: 53 (30-74)
Koukourou, Australia, 2001[48]	male with primary inguinal hernia, age 18-90, support at home for post-op care, telephone available, ASA grade 1 or 2	Recurrent hernia and inguinoscrotal hernias	Nylon darn vs polypropylene mesh (technique undisclosed)	1 , 6 weeks and 1 year	n= 51 %male: 100 age: 56 ± 18	n= 54 %male: 100 age: 53 ± 19

McGillicuddy, Canada, 1998[49]	Male patients with inguinal hernia, 20-90 years old	Patients who chose laprascopic technique	Shouldice vs. Lichtenstein with polypropylene (Marlex, Trilex)	1, 4, 52 weeks, 1, 2, 3, 4 years	n= 337 %male: 100 age: NR	n= 371 %male: 100 age: NR
Memon, Pakistan, 2017[50]	Male patients, age of 20-60 years who reported direct or indirect inguinal hernia repair with open herniotomy and hernioplasty or herninorraphy	ASA class IV or above, malignancy or gangrenous bowls as content of sac, recurrent inguinal hernia or ascites	Darn repair vs. Lichtenstein with synthetic mesh	every month for 1 year	n= 46 %male: 100 age: 54.3	n= 46 %male: 100 age: 52.3
Miedema, USA, 2003[51]	NR	Younger than 18, female, use of systematic steroids, an incarcerated hernia, recurrent hernia, a collagen and vascular disease, ASA score of IV or V, an allergy to acetaminophen or codeine	Shouldice vs. Lichtenstein with polypropylene (Marlex)	1,3,6-9 years	n= 52 %male: 100 age: 62 (28–79)	n= 49 %male: 100 age: 63 (40–81)
Miedema, USA, 2003[51]	NR	Younger than 18, female, use of systematic steroids, an incarcerated hernia, recurrent hernia, a collagen and vascular disease, ASA score of IV or V, an allergy to acetaminophen or codeine	McVay vs. Lichtenstein with polypropylene (Marlex)	1,3,6-9 years	n= 49 %male: 100 age: 65 (40–87)	n= 49 %male: 100 age: 63 (40–81)
Nordin, Sweden, 2002[39]	Men, 25-75 years old, clinically manifest, unilateral primary inguinal hernia	irreducibility, femoral hernia,coagulation abnormalities, anticoagulant treatment, unsuitable for anaesthesia	Shouldice vs Lichtenstein	8 weeks, 1, 3 years	n= 148 %male: 100 age: NR	n= 149 %male: 100 age: NR

Szopinski, Poland, 2012[52]	Adult male patients with primary inguinal hernia, patients with bilateral hernias were included but only one side was operated on	Patients with an aponeurosis that was divided, tiny, and/or weak. Recurrent or strangulated hernias or mental disorder, ASA scale at>3, history of forced hernia reduction with subsequent hospitalization, a history of infection, or presence of any scar in groin region	Darn repair (Desarda) vs Lichtenstein with Prolene	1, 2, 3 years	n= 105 %male: 100 age: 50.2 ± 17.5	n= 103 %male: 100 age: 54.1 ± 15.3
Wamalwa, Kenya 2015[53]	Men between 18 and 80 years with clinically manifest, unilateral and primary inguinal hernia	Irreducibility, femoral hernia, coagulation abnormalities, anticoagulant treatment and patients for whom anaesthesia was unsuitable	Shouldice vs. Lichtenstein with Prolene	24 hours, 2weeks, 3 month and 1, 2 years	n= 22 %male:100 age: 63.5 (25-76)	n= 23 %male:100 age: 60 (22-80)

Table A2: Characteristics of Synthetic Mesh vs. Porcine Mesh Studies Included in the Inguinal Hernia Review

Author, Country, Year	Inclusion criteria	Exclusion criteria	Control vs intervention	Follow-up times	Control patient characteristics	Intervention patient characteristics
Ansaloni Italy 2009[57]	18 years old or older, noncomplicated primary inguinal hernia, Gilberta I-VI, ASA I-III, informed consent	recurrent hernia, condition preventing evaluation of pain, hypersensitivity to drugs used in study, intraoperative findings of pathologies other than hernia	Surgisis Inguinal Hernia Matrix vs polypropylene	1 week, 1, 3, 6 months, 1, 3 years	n= 35 %male: 100 age: 56.2 18.0	n= 35 %male: 100 age: 61.3 17.7
Ansaloni Italy 2003[56]	19 years old or older, noncomplicated primary inguinal hernia, Gilberta I-VI, ASA I-III, informed consent	recurrent hernia, condition preventing evaluation of pain, hypersensitivity to drugs used in study, intraoperative findings of pathologies other than hernia	Surgisis Gold Soft Tissue Graft vs polypropylene	1 week, 1, 6 months	n= 12 %male: 100 age: NR	n= 8 %male: 100 age: NR
Bellows, USA 2013[58]	Adult males greater or equal to 18 years of age with a primary non-emergent inguinal hernia	Recurrent hernias, any condition preventing a correct evaluation of pain, hypersensitivity to any drug in study, intra-operative findings of different pathology.	Strattice Tissue Matrix (porcine) vs Lichtenstein with UltraPro	10 days, 3 months, 1 and 2 year	n= 84 %male: 100 age: 56 ± 15	n= 88 %male: 100 age: 57 ± 14
Bochicchio, USA, 2014[55]	Male, 18 years or older, had a diagnosis of unilateral inguinal hernia and provided written informed consent	ASA class IV or class V, contradictions to general anesthesia, bowel obstruction, bowel strangulation, peritonitis, bowel perforation, local or systemic infection, a history of inguinal hernia repair with mesh	Inguinal Hernia Matrix (biograft) vs Lichtenstein with polypropylene	2 weeks, 3,6 months and 1 year	n= 50 %male: 100 age: 64 (24-85)	n= 50 %male: 100 age: 59 (25-87)

Appendix 3: Meta-Analysis Forest Plots

Figure A1: Forest Plot of Infection in Inguinal Hernia Patients with Synthetic Mesh vs. Suture Repair

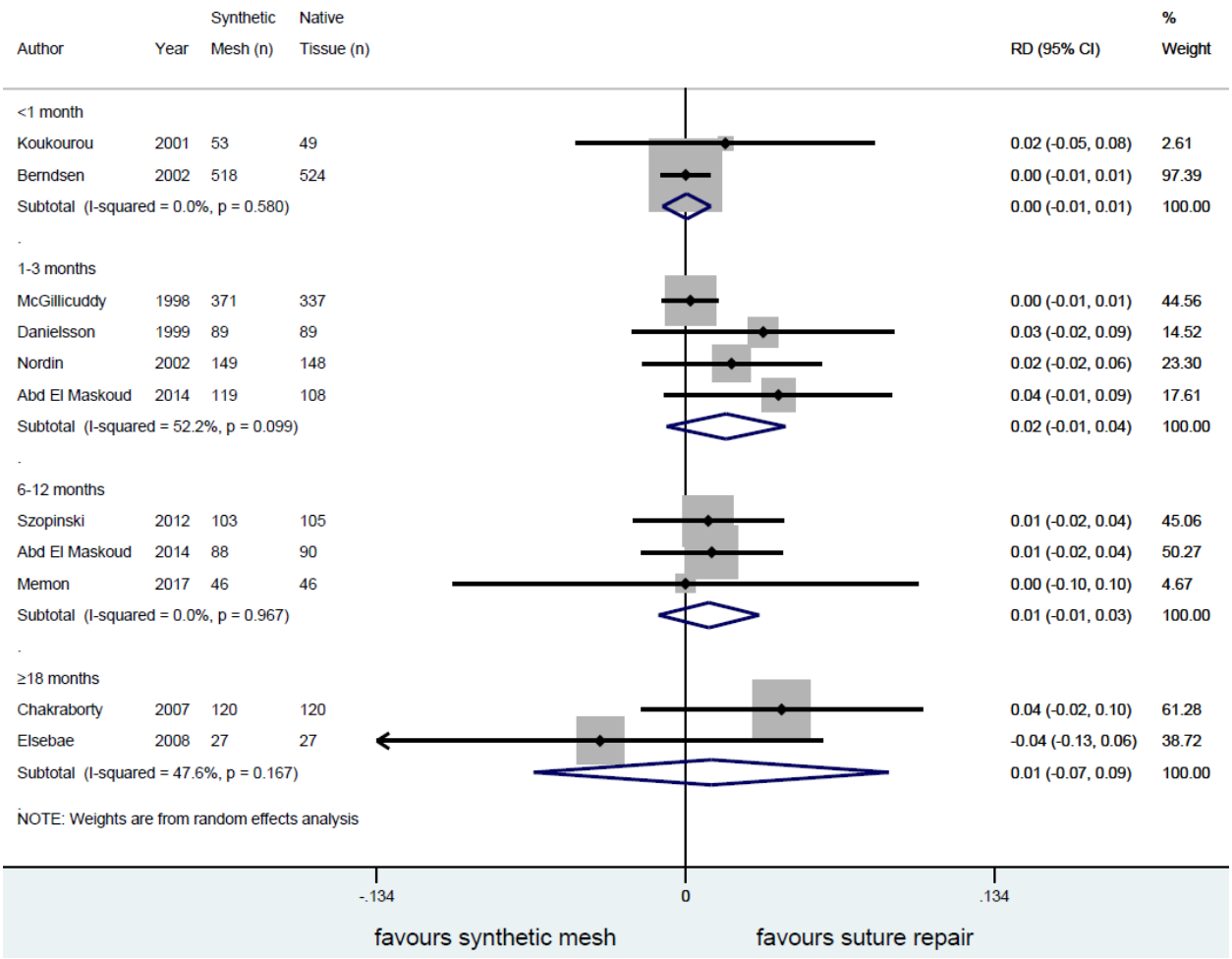

Figure A2: Forest Plot of Pain in Inguinal Hernia Patients with Synthetic Mesh vs. Suture Repair

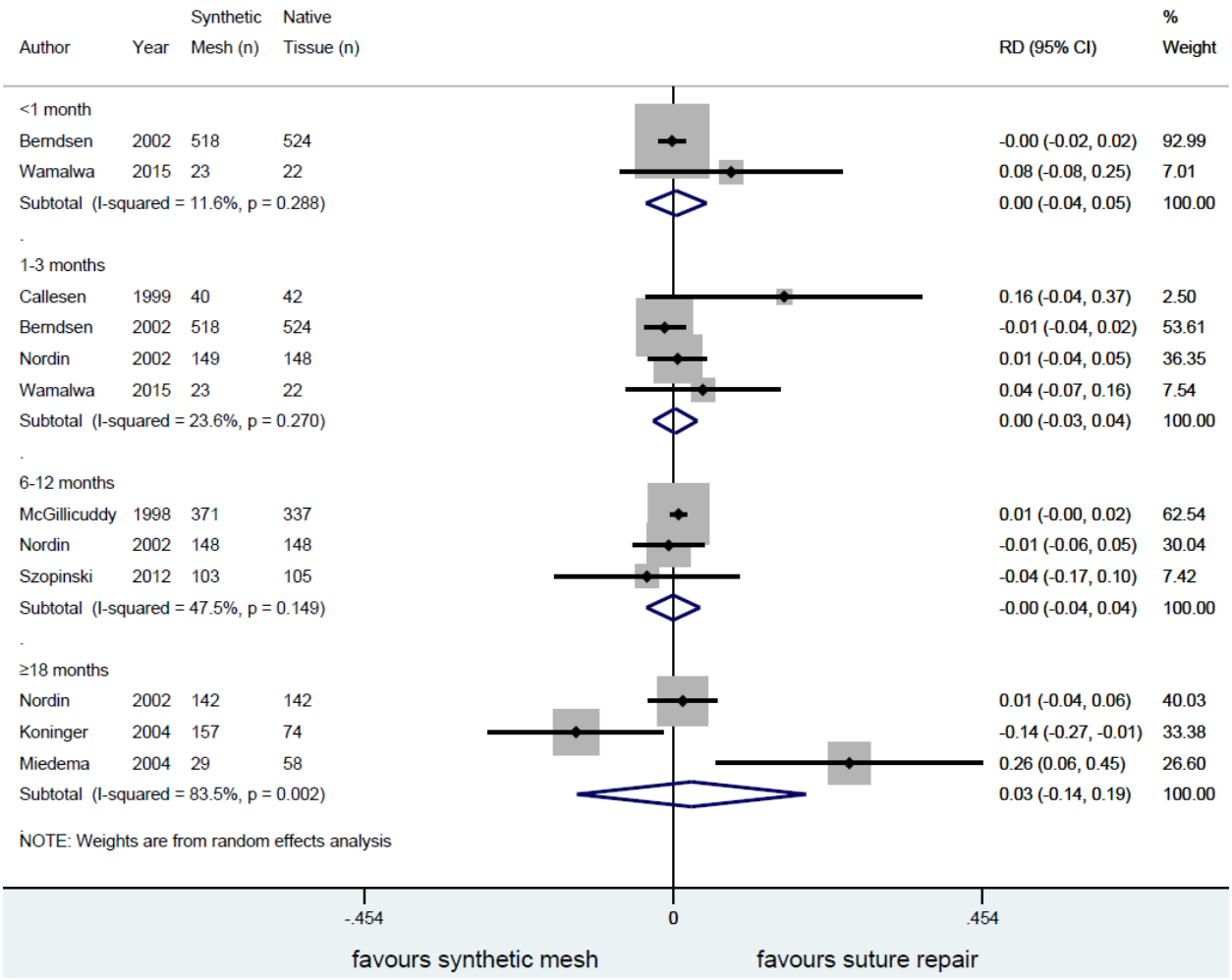

Figure A3: Forest Plot of Hematoma in Inguinal Hernia Patients with Synthetic Mesh vs. Suture Repair

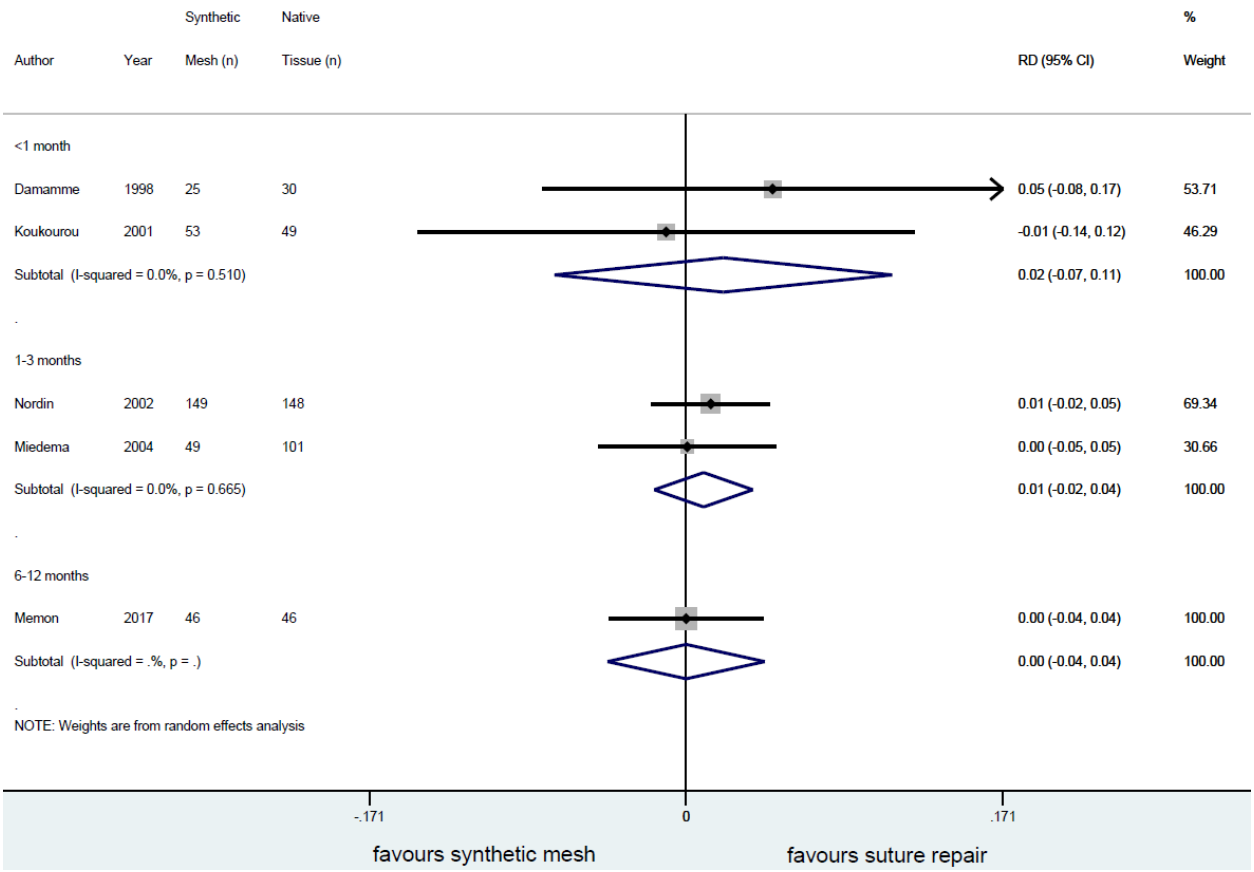

Figure A4: Forest Plot of Seroma in Inguinal Hernia Patients with Synthetic Mesh vs. Suture Repair

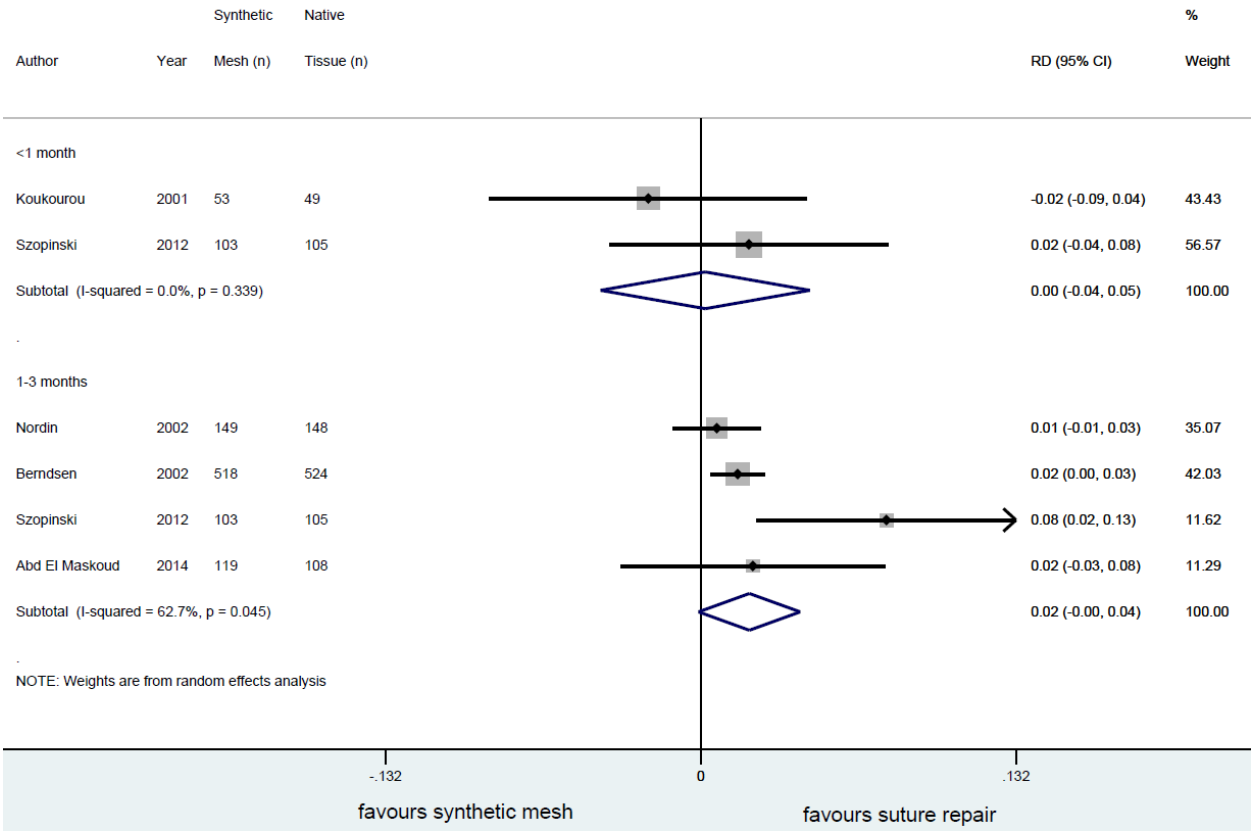

Figure A5: Forest Plot of Testicular Atrophy in Inguinal Hernia Patients with Synthetic Mesh vs. Suture Repair

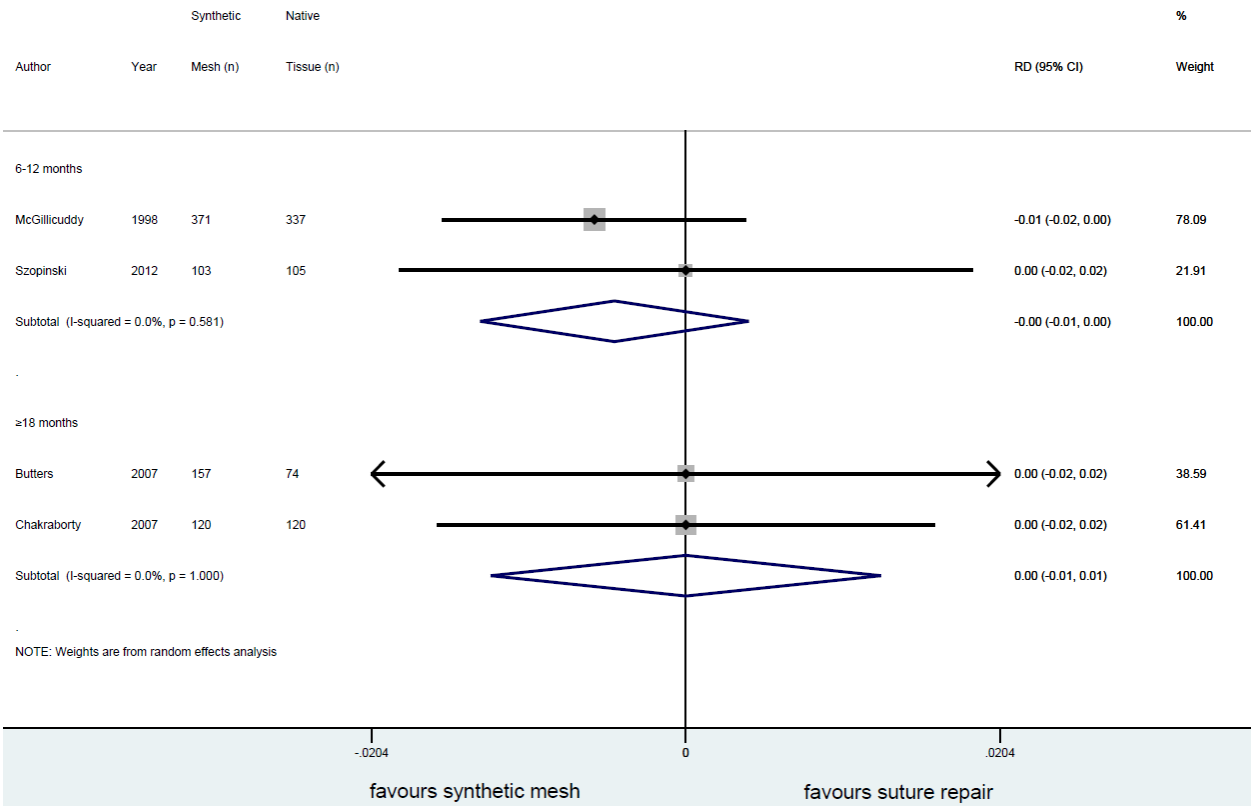

Figure A6: Forest Plot of Urinary Retention in Inguinal Hernia Patients with Synthetic Mesh vs. Suture Repair

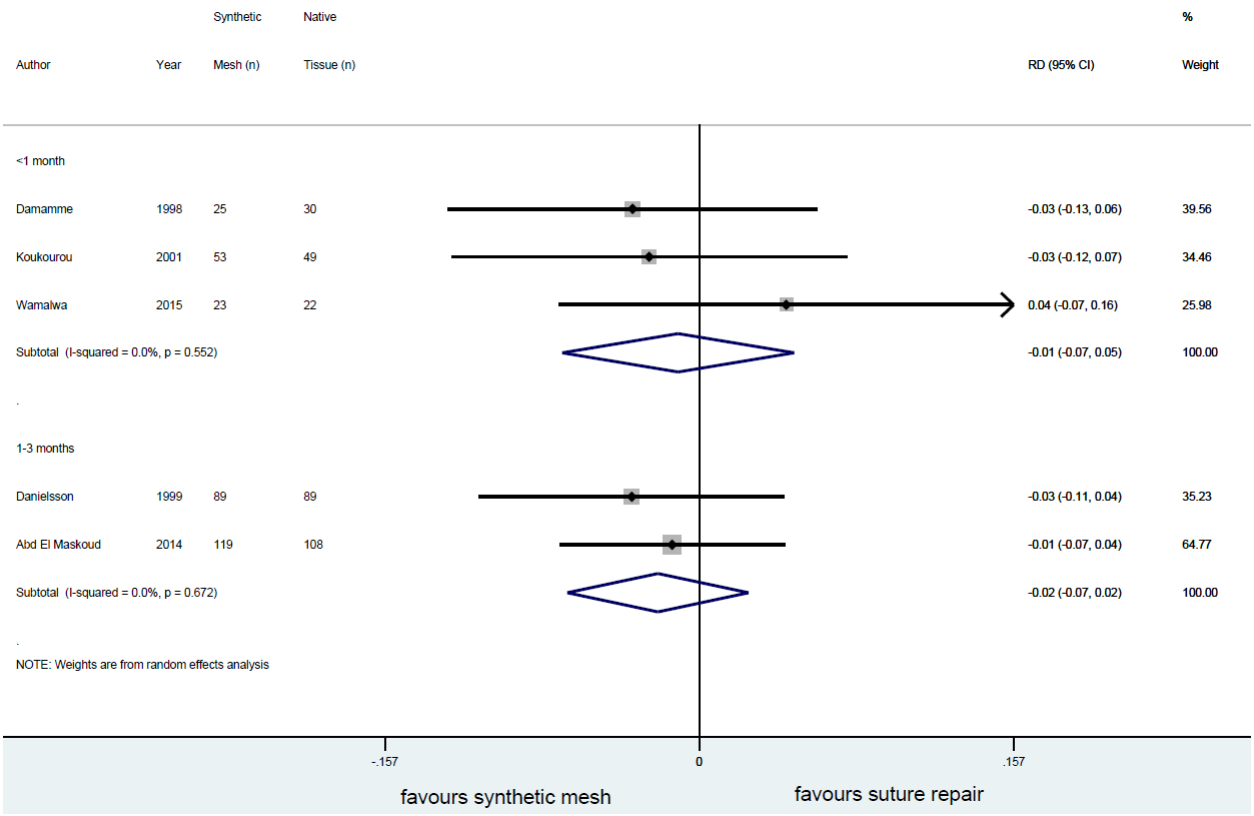

Figure A7: Forest Plot of Neurological Complications in Inguinal Hernia Patients with Synthetic Mesh vs. Suture Repair

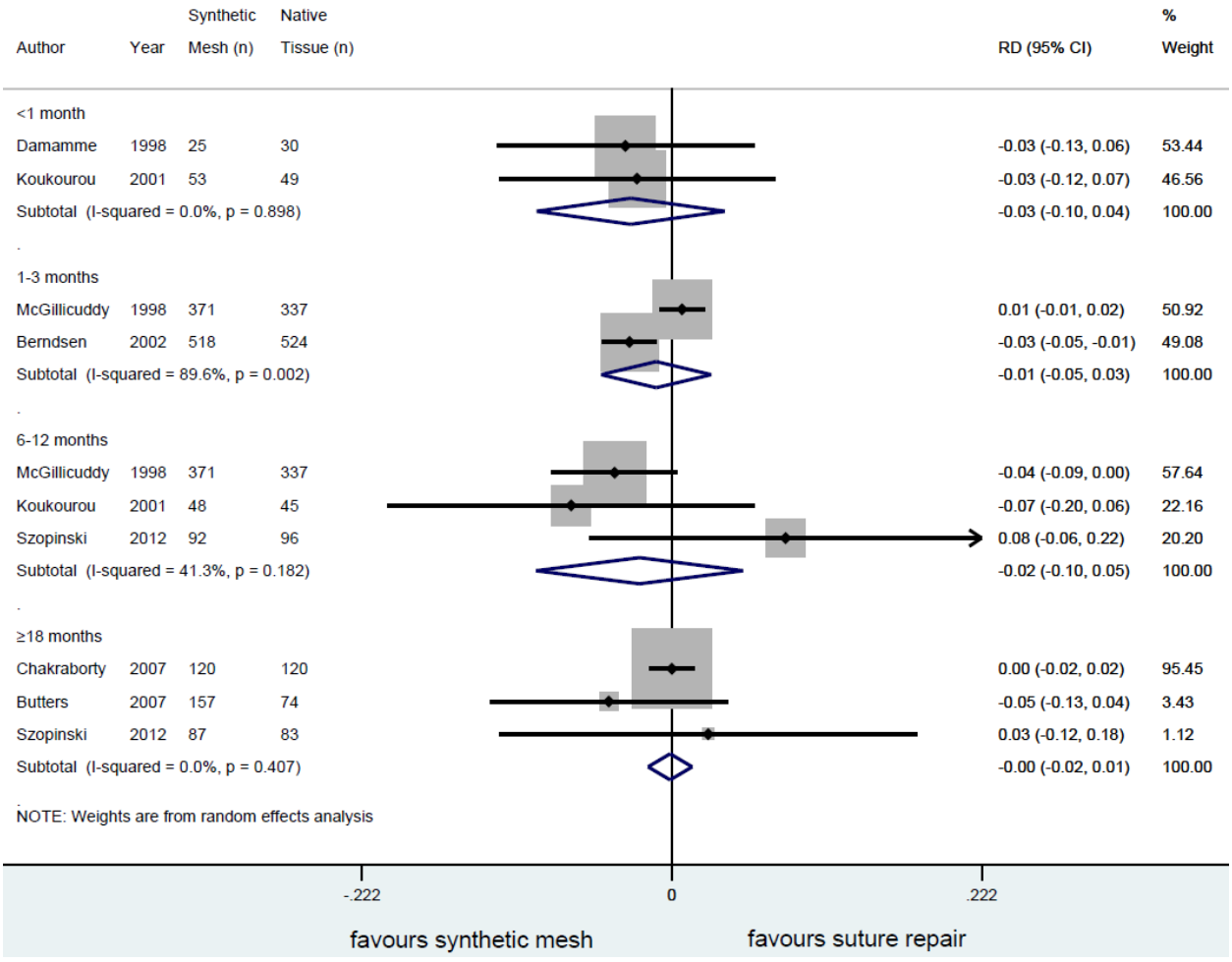

Figure A8: Forest Plot of Infection in Inguinal Hernia Patients with Synthetic Mesh vs. Porcine Mesh

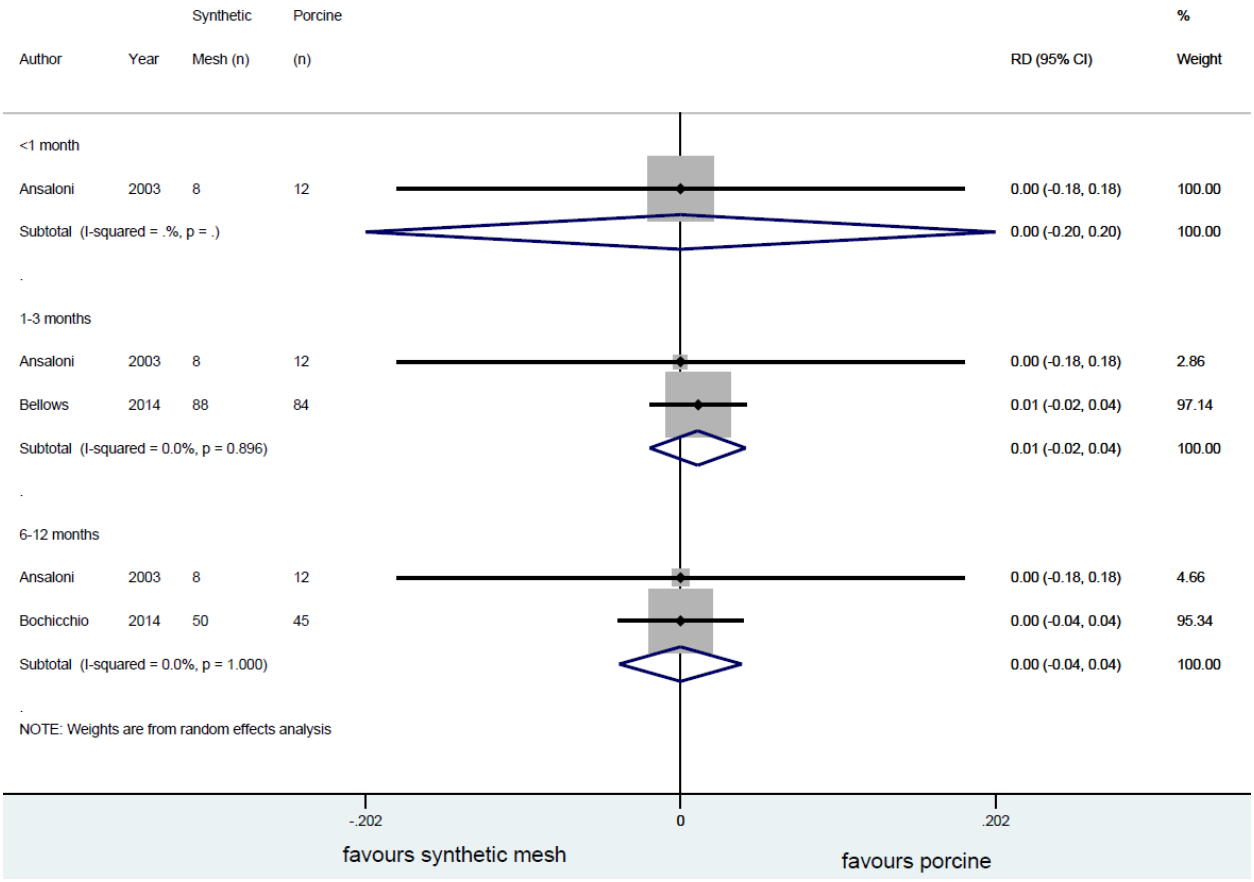

Figure A9: Forest Plot of Pain in Inguinal Hernia Patients with Synthetic Mesh vs. Porcine Mesh

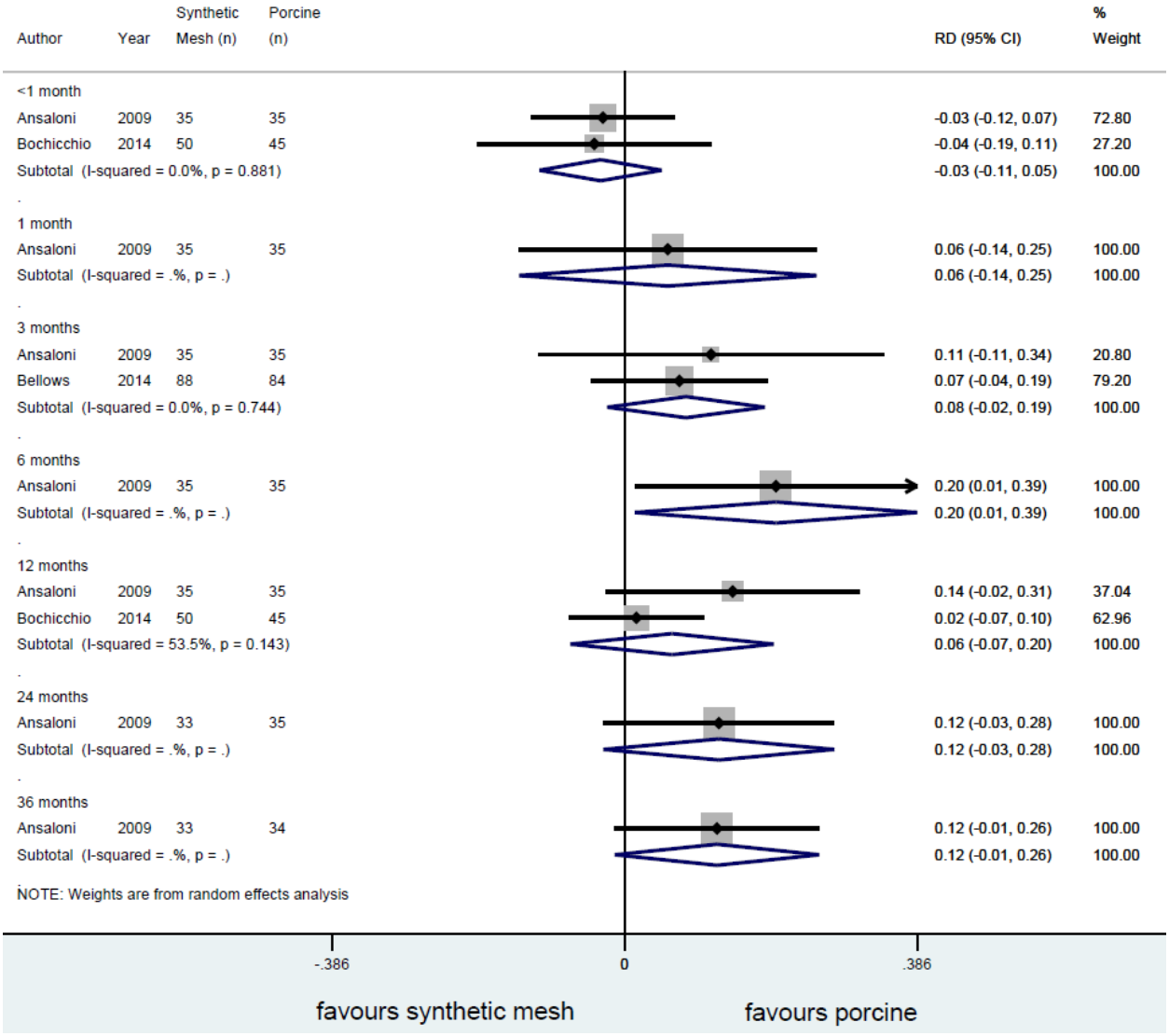

Figure A10: Forest Plot of Hematoma in Inguinal Hernia Patients with Synthetic Mesh vs. Porcine Mesh

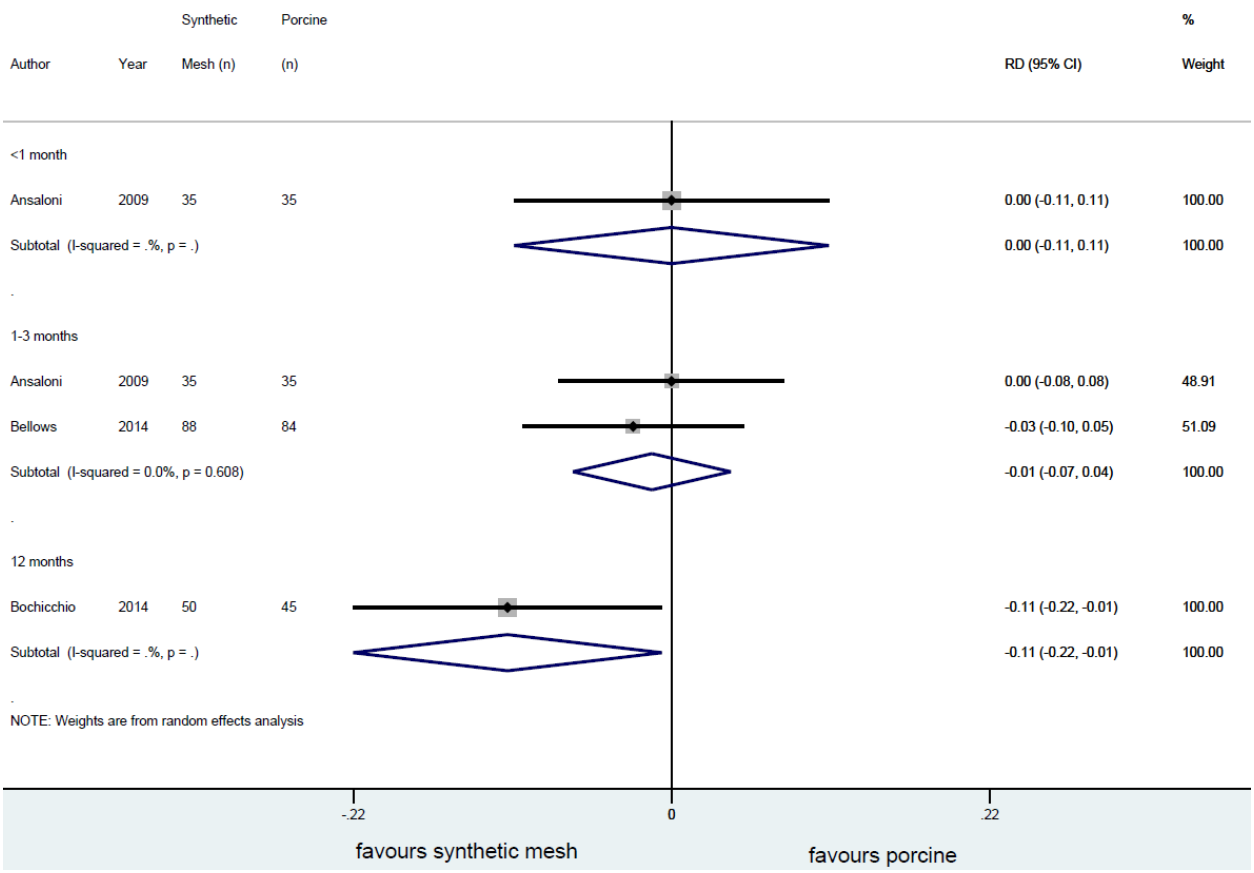

Figure A11: Forest Plot of Seroma in Inguinal Hernia Patients with Synthetic Mesh vs. Porcine Mesh